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NATO Committee on the Challenges of Modern Society

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AIR QUALITY CRITERIA
FOR
SULFUR OXIDES

A Report By CCMS/NATO Expert Panel
On
Air Quality Criteria

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November 1971

FOREWORD

The material presented in this document represents a first attempt by the Expert Panel for Air Quality Criteria, Committee on Challenges to Modern Society, NATO, to compile a compendium of information using the United States Air Quality Criteria for Sulfur Oxides as a basic document on the effects of oxides of sulfur in the ambient air on man, materials, vegetation, and weather. Definitive, quantitative relationships between concentration of oxides of sulfur and consequent effects are not well established. In years past, concern over these detrimental effects has been limited, although some notable scientific investigations were undertaken. Recent interest and activity on the part of the public, governmental, scientific, academic, and industrial sectors of our communities have stimulated research on the effects of pollution on man and his environment. The result is an ever-increasing body of knowledge that must be analyzed, interpreted, and finally expressed as information supporting or refuting suggested criteria. The assimilation of this new knowledge is not a task that can be undertaken by a small body of men--such as a committee of this nature. Rather, the responsibility for assuring that criteria continually reflect the most significant information available rests with those same sectors of our communities that have inspired all of us to strive to improve our environment--the public, the government, the scientific, the academic, and the industrial sectors.

The Panel encourages and welcomes new data, comments, and constructive criticism of this document. We suggest that a procedure be established whereby this document and documents to follow can be revised and updated periodically.

For the Expert Panel,
R. E. Engel, Ph.D., Chairman

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The working panel which worked diligently through the course of the year receives the highest praise. The panel members were:

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Dr. F. Gordon Hueter, USA
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Ronald E. Engel, Ph.D.
Panel Chairman

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Chapter 1

PHYSICAL AND CHEMICAL PROPERTIES AND THE ATMOSPHERIC REACTIONS OF THE OXIDES OF SULFUR

A. INTRODUCTION

Sulfur dioxide, sulfur trioxide, and the corresponding acids and salts (sulfites and sulfates) are common atmospheric pollutants which arise mainly from combustion processes. Under normal conditions, the predominant state is gaseous sulfur dioxide, together with smaller amounts of nonvolatile sulfuric acid mist or sulfate salts. In this chapter, the chemical and physical properties of these substances are discussed in relation to their chemical reactions in the atmosphere. Treatments of the chemistry of sulfur oxides are to be found in most works on inorganic chemistry (e.g., references 1 and 2).

Since the proper and efficient establishment of criteria and standards ultimately depends upon reliable analytical data, it is particularly important that proper attention be given to (1) the sampling techniques and (2) the analytical procedures employed. These have been reviewed by Hendrickson,[3] Katz,[4] and more recently by Stevens.[5]

A companion document to this publication, Guidelines to Assessment of Air Quality, discusses in detail recommended procedures and techniques. Numerous data on the sources and methods of measuring ambient concentrations of sulfur oxides in the Federal Republic of Germany are given in the "Rules of the VDI Commission 'Control of Air Pollution.'"[6]

B. OCCURRENCE

The oxides SO_2 (sulfur dioxide) and SO_3 (sulfur trioxide), with the corresponding acids H_2SO_3 (sulfurous acid) and H_2SO_4 (sulfuric acid) and the salts of these acids, are well known in atmospheric studies.

Solid and liquid fossil fuels generally contain appreciable quantities of sulfur, usually in the form of inorganic sulfides and/or sulfur-containing organic compounds. Combustion of the fuel in power plants forms sulfur oxides in the ratio of 40 to 80 parts of sulfur dioxide to 1 part of sulfur trioxide. Since oxides of sulfur occur naturally only in minute amounts, the burning of fossil fuels such as coat and petroleum constitutes the major source of sulfur oxides in the global atmosphere.

Additional pollution results from the refining of petroleum, the smelting of ores containing sulfur, the manufacture of sulfuric acid, the burning of refuse, paper making, and the burning or smoldering of coal refuse banks.[7] In all of these processes, a small amount of sulfur trioxide or sulfuric acid also is emitted. Sulfur trioxide is normally present in the atmosphere in extremely small concentrations because it is converted to sulfuric acid soon after its entry into the atmosphere.

Of considerable importance to the meteorological and chemical behavior of sulfur oxides in the atmosphere, as well as to their measurement, are the kinds of emitters, whether large or small and whether disperse or point sources. The trend of operations has been away from sulfur dioxide pollution by low-level disperse sources and toward large point sources, except for space heating and diesel trucks using fuels of high sulfur content. The large source emissions contain lower concentrations of polynuclear aromatic hydrocarbons and higher concentrations of nitrogen oxides and sulfuric acid. Particulate matter, which interacts with the oxides of sulfur, can be controlled to a greater extent when emitted from the larger sources. Further, emissions from

Table 1-1. HEMISPHERIC SO_2 POLLUTANT EMISSIONS'

(10^6 tons)

Source	Total SO_2	Northern Hemisphere	Southern Hemisphere
Coal[14]	102	98 (96%)	4 (4%)
Petroleum[14] Comb. and Refin.	28.5	27.1 (95%)	1.4 (5%)
Smelting[15]			
Copper	12.9	8.6 (67%)	4.3 (33%)
Lead	1.5	1.2 (80%)	0.3 (20%)
Zinc	1.3	1.2 (90%)	0.1 (10%)
Total	146	136 (93%)	10 (7%)

large sources usually are emitted from high stacks, a practice that appears to reduce average ground level concentrations and the frequency of air pollution episodes.[8-13]

Sources of atmospheric sulfur oxides can be considered from the viewpoint of their annual production. Obviously, sulfur-containing coal and fuel oil utilized for heating during the winter will produce a seasonal increase in atmospheric SO_2. This is in contrast with industrial sources, such as power stations and factories, whose effluents are more or less constant throughout the year.

Major worldwide sources of SO_2 emissions are tabulated in Table 1-1.[14,15]

C. PHYSICAL PROPERTIES OF SULFUR DIOXIDE

Sulfur dioxide is a nonflammable, nonexplosive, colorless gas. In concentrations above 0.8 to 2.7 mg/m^3 (0.3 to 1 ppm) in air, most people can detect it by taste; in concentrations greater than 8.1 mg/m^3 (3 ppm) it has a pungent, irritating odor.[16-19] The gas is highly soluble in water: 11.3 g/100 ml at 20°C, as compared to 0.004, 0.006, 0.003, and 0.169 g/100 ml for oxygen, nitric oxide, carbon monoxide, and carbon dioxide, respectively. The physical properties of sulfur dioxide are listed in Table 1-2.

Table 1-2. PHYSICAL PROPERTIES OF SULFUR DIOXIDE

Molecular weight	64.06
Density (gas), g/liter	2.927 at 0°C; 1 atm
Specific gravity (liquid)	1.434 at -10°C
Molecular volume (liquid), ml	44
Melting point, °C	-75.46
Boiling point, °C	-10.02
Critical temperature, °C	157.2
Critical pressure, atm	77.7
Heat of fusion, Kcal/mole	1.769
Heat of vaporization, Kcal/mole	5.96
Dielectric constant (practical units)	13.8 at 14.5°C
Viscosity, dyne sec/cm^2	0.0039 at 0°C
Molecular boiling point constant, °C/1000g	1.45
Dipole moment, Debye units	1.61

D. CHEMICAL PROPERTIES OF SULFUR DIOXIDE AND SULFUROUS ACID

Sulfur dioxide is a gas under ambient atmospheric conditions. It can act either as a reducing agent or as an oxidizing agent. Of considerable importance to the problem of air pollution is the ability of the gas to react either photochemically or catalytically with materials in the atmosphere to form sulfur trioxide, sulfuric acid, and salts of sulfuric acid. These atmospheric reactions are discussed separately in Section G.

Sulfur dioxide may act as an oxidizing or as a reducing agent at room temperature. For example, sulfur dioxide oxidizes hydrogen sulfide to form elemental sulfur and water.

$$2H_2S + SO_2 \longrightarrow 3S + 2H_2O. \qquad (1\text{-}1)$$

As a reducing agent, the gas reacts very slowly with oxygen at 400° C to yield sulfur trioxide, but catalytic oxidation to sulfur trioxide occurs at temperatures as low as room temperature.

$$SO_2 \xrightarrow[\text{catalyst}]{1/2\ O_2} SO_3. \qquad (1\text{-}2)$$

Catalysts effective in this oxidation include finely divided platinum, charcoal, vanadium pentoxide, graphite, chromic oxide, ferric oxide, and the nitrogen oxides. The nitrogen oxides are used as the catalyst in the chamber process of manufacturing sulfuric acid from sulfur dioxide.

Sulfur dioxide also acts as a reducing agent in aqueous solution. The reaction with iodine, for example, yields sulfate and iodine ions and the decolorization of a starch-iodine mixture is used in one of the methods for determing atmospheric SO_2.

Lead peroxide (PbO_2) is an active oxidizing agent and is used to obtain an estimate of the amount of oxidizable sulfur compounds in air, e.g.,

$$PbO_2 + SO_2 \longrightarrow PbSO_4 \qquad (1\text{-}5)$$

Hydrogen peroxide (H_2O_2) is used extensively as an oxidizing agent in the analysis of air samples for sulfur dioxide: sulfuric acid is formed, and is estimated conductometrically or by titration.

Sulfur dioxide reacts with water to form sulfurous acid (H_2SO_3)

$$SO_2 + H_2O \rightleftarrows H_2SO_3. \qquad (1\text{-}6)$$

The pure acid is unstable and exists only in aqueous solution. Sulfurous acid can react directly with many organic dyes. The West-Gaeke method for the determination of atmospheric sulfur dioxide takes advantage of this property; pararosaniline is used as the organic dye.

E. PHYSICAL AND CHEMICAL PROPERTIES OF SULFUR TRIOXIDE

Sulfur trioxide in ambient air is derived either from combustion sources directly or from the oxidation of atmospheric sulfur dioxide. Sulfur trioxide may exist in the air as a vapor if the water vapor concentration in the air is low enough; but if sufficient water vapor is present (as there probably always is in ambient air), the sulfur trioxide combines immediately with water to yield sulfuric acid in the form of droplets.

$$SO_3 + H_2O \longrightarrow H_2SO_4 \tag{1-7}$$

Sulfuric acid, rather than sulfur trioxide, is thus the compound normally found in the atmosphere. Because of the difficulty of measuring free sulfur trioxide in the air, little is known about how much may be present under various circumstances; presumably, it is present in the unhydrated form only in trace amounts.

Sulfur trioxide readily converts basic oxides to sulfates. It is also a dehydrating agent. When phosphates, carbonates, perchlorates, and salts of other oxy-acids react with sulfur trioxide, the corresponding anhydride of the oxy-acid is formed. Sulfur trioxide may also act as an oxidizing agent, giving free halogens (except fluorine) with many metal and nonmetal halides. Gilbert[20] recently reviewed the numerous and diverse reactions of sulfur trioxide with organic compounds.

F. ATMOSPHERIC REACTIONS OF SULFUR OXIDES

1. Laboratory Investigations

Sulfur dioxide is oxidized in the atmosphere by two main processes: photochemical and catalytic. Junge and Ryan[21] studied the oxidation of sulfur dioxide in solution and found that essentially no reaction occurred in the absence of a catalyst. When ferric chloride was used as a catalyst, oxidation did take place. The final amount of sulfate formed was only slightly dependent on the concentration of catalyst but was a linear function of sulfur dioxide concentration. Johnstone and Coughanowr[22] estimated from their study of sulfur dioxide oxidation in small droplets that, if manganese sulfate were present as 1-micrometer crystals, the oxidation rate in fog droplets at 2.7 mg/m^3 (1 ppm) SO_2 would be about 1 percent per minute. Both investigators found that manganese salts were more effective catalysts than iron salts. Bracewell and Gall[23] also measured rates of catalytic oxidation of sulfur dioxide in droplets and estimated that, in the presence of ferric or manganous ions, rates of oxidation could be sufficient to account for the sulfuric acid content of urban fogs, assuming sulfur dioxide concentrations of 1750 $\mu g/m^3$ or about 0.6 ppm (see appendix for conversion factors).

The oxidation of sulfur dioxide essentially stopped when the pH of the water droplets decreased to about 2 in Junge and Ryan's experiments,[21] and they suggested that the effect is due, at least in part, to the low solubility of sulfur dioxide in strongly acidic solutions. If ammonia was present in the air to neutralize the acid as it was formed, oxidation of sulfur dioxide continued. Van den Heuvel and Mason[24] found that for given concentrations of ammonia and sulfur dioxide the mass of sulfate formed was proportional to the product of the surface area of the drops and the time of exposure.

The catalytic oxidation of sulfur dioxide may also proceed after adsorption of the gas on the surfaces of suspended solid particles. Smith et al.[25] demonstrated preferential chemisorption of sulfur dioxide at ambient concentrations on iron oxide and aluminum oxide aerosols followed by multilayered physical adsorption at higher concentrations. Liberti and Devitofrancesco[26] were unable to desorb sulfur dioxide from atmospheric dust samples and concluded from analyses of these samples that adsorbed sulfur dioxide is either oxidized to sulfate or reacts to form a variety of organic compounds. The interaction of sulfur dioxide with atmospheric aerosols is important also from the point of view of the toxicological effects of such pollutant combinations (see Chapter 7).

Gerhard and Johnstone[27] found the photooxidation rate of sulfur dioxide in air and sunlight to be 0.1 to 0.2 percent per hour; the rate did not depend upon the presence of sodium chloride nuclei or nitrogen dioxide, nor on changes of relative humidity from 30 to 90 percent. Renzetti and Doyle[28] found appreciable formation of H_2SO_4 aerosol by irradiation, at 3130 Å, of sulfur dioxide at concentrations below 1.7 mg/m^3 (1 ppm) and at relative humidity below 50 percent. More recently Urone et al.[29] investigated reactions of sulfur dioxide in air in the presence of water vapor with irradiation at 3100 Å-4200 Å; their results indicated a faster photooxidation rate when hydrocarbon and nitrogen dioxide are present.

Of primary interest in the photochemical oxidation of sulfur dioxide is the formation of particulate matter in hydrocarbon-nitrogen oxides systems. In the absence of sulfur dioxide, little or no aerosol is formed when mixtures of nitrogen oxides and most hydrocarbons (all at atmospheric concentrations) are irradiated. (Varying amounts of particulate matter, however, are formed when nitrogen oxides are irradiated with any of several hydrocarbons such as cyclic olefins.)[30-32] In the absence of nitrogen oxides, Johnstone and Dev Jain[33] obtained particulate matter when they irradiated sulfur oxide with n-butane both at 20 mm Hg partial pressure; but Kopczynski and Altshuller[34] were unable to detect any formation of particulate matter when sulfur dioxide at atmospheric concentration together with atmospheric concentrations of either olefins or paraffins were irradiated. In fact, Renzetti and Doyle[28] and Dainton and Ivin[35] demonstrated that olefins can suppress the production of particulate matter during irradiation of sulfur dioxide in the absence of nitrogen oxides.

On the other hand, mixtures of olefins, nitrogen dioxide, and sulfur dioxide definitely form an aerosol in the presence of sunlight. Thus a major product of the complex photochemical reaction is sulfuric acid,[28,36-38] which is a hygroscopic material forming light-scattering droplets of sulfuric acid mist. The optical density of such a haze obviously will depend on the prevailing relative humidity. Sulfuric acid is sufficiently nonvolatile to self-nucleate even at realistic atmospheric concentrations but this may not be necessary in view of the larger numbers of nuclei present even in "clean" air. The exact mechanism by which sulfur dioxide is converted to sulfuric acid mist remains unclear.

Even more uncertain is the chemical nature of the aerosol reportedly formed in hydrocarbon-nitrogen oxide systems without sulfur dioxide.

Because of the complexities of the reactions, no mechanism put forth since the work of Schuck and Doyle[30] and Renzetti and Doyle[28] has extended knowledge of the photochemistry of sulfur oxides. For detailed reviews of photochemical air pollution, the work of Leighton,[39] Altshuller and Bufalini,[40] and Stern[41] should be consulted. The basic spectroscopy and photochemistry of sulfur dioxide are discussed by Calvert and Pitts.[42]

2. Field Investigations

Gartrell et al.[43] studied the oxidation of sulfur dioxide in coal-burning power plant plumes. Soluble sulfates were collected on membrane filters, and sulfur dioxide was collected in hydrogen peroxide. The sulfur trioxide concentration in the stack gas was 40 to 108 mg/m^3 (15 to 40 ppm) and the sulfur dioxide concentration was about 5.9 g/m^3 (2200 ppm). Thus, on a weight basis, the ratio of sulfuric acid to sulfur dioxide was initially about 0.03. In successive samples collected from the plume, the investigators found oxidation rates ranging from zero to 2 percent per minute. Increasing rates of oxidation were observed with increasing relative humidity, and the investigators concluded that moisture within the plume of the ambient strata was the most important factor affecting the rate of oxidation.

Weber[44] estimates that 50 percent of emitted sulfur dioxide from power plants and space heating is lost from the atmosphere through oxidation within 20 to 30 minutes, subject to meteorogical conditions. Periods of high atmospheric relative humidity are most favorable for oxidation losses.

Weber's results apply in the immediate vicinity (less than 10 kilometers) of the sulfur dioxide source. On a space scale the size of the United States, Junge[45] estimates the residence time of industrially produced sulfur dioxide to be approximately five days.

Katz[46] made simultaneous collections of two air samples in the Sudbury, Ontario, nickel-smelting area to determine sulfur dioxide and "total sulfur contaminants," which he interpreted as sulfur dioxide, sulfur trioxide, and sulfuric acid. Although reservations exist about the quantitative nature of the data because of a number of apparently uncontrolled or uncontrollable parameters in the experiments, they nevertheless indicate qualitatively that sulfur dioxide is oxidized in the atmosphere. Analysis of the data presented by Katz shows that over relatively narrow range of conditions studied the rate of decrease in the ratio of sulfur dioxide to total sulfur contaminants appears to be independent of concentration of contaminants, of the time of day at which the measurements were made, and of ambient temperature. The rate was about 0.035 percent per minute.

This rate, obtained from the work of Katz, is much smaller than that reported by Gartrell and associates,[43] perhaps in part because Gartrell had more efficient sulfuric acid collection and perhaps in part because atmospheric conditions were not the same. As noted previously, Gartrell and his associates concluded that moisture within the plume of the ambient air strata is the primary rate-determining factor in the oxidation.

The effect of concentration on reaction rate also must be considered. Whereas Katz' data indicated that the rate of loss of sulfur dioxide was independent of concentration, the sulfur dioxide concentrations of the samples (taken in the open air) generally were less than 5.4 mg/m^3 (2 ppm).

Although Gartrell et al. did not indicate concentrations of the contaminants in their plume samples, concentrations in such a plume would be much higher than 2.7 to 5.4 mg/m^3 (1 to 2 ppm); at the higher concentrations the reaction rate may be faster and concentration dependent.

3. Particulate Sulfate in Polluted Air

The oxidation of atmospheric sulfur dioxide results in the formation of sulfuric acid and other sulfates that typically account for about 5 to 20 percent of the total suspended particulate matter in urban air. In general, as expected, there is a relationship (Commins;[47] see also Chapter 2, Section C) between the concentrations of sulfuric acid or sulfate and sulfur dioxide.

In recent years, some studies have been made of the particle size distribution of suspended atmospheric sulfate. This property determines visibility reduction[48] and is also an important factor in physiological responses because of its relation to the degree of penetration and retention of particles in lungs. Roesler et al.[49] reported sulfate size distributions in downtown Chicago and Cincinnati based on 24-hour samples collected with cascade impactors. They found values for mass median diameter (MMD), i.e., for equivalent spheres of unit density, that average 0.3 to 0.4 micrometers in the two cities. These were within the range of average MMD value for total sulfur (0.2 to 0.9 micrometer) found by Ludwig and Robinson[50] in the Los Angeles and San Francisco Bay areas. From 8-hour samples collected continuously for a week in each of four cities, Wagman et al.[51] found values for average sulfate MMD (i.e., 0.42 micrometer in Chicago, Cincinnati, and Fairfax, and 0.60 micrometer in Philadelphia) that were in good agreement with these measurements.

They also found that sulfate particle sizes generally increased with increasing relative humidity, whereas sulfate concentration was more closely correlated with absolute humidity. Of particular significance is the fact that all of these investigations showed that a major fraction (generally 80 percent or more) of urban atmospheric sulfate is associated with particles below 2 micrometers in diameter. Suspended sulfate is therefore largely in the respirable fraction of particulate matter and is associated mainly with particles that cause the most pronounced reduction in visibility.

G. EFFECTS OF SULFUR OXIDES ON LIGHT TRANSMISSION IN ATMOSPHERE

One of the most noticeable physical effects of air pollution is the reduced visibility in polluted atmospheres. Comprehensive treatments of the subject include those of Steffens,[52] Middleton,[48] and Robinson.[53] A companion document, Air Quality Criteria for Particulate Matter, also discusses the subject in Chapter 3, "Effects of Atmospheric Particulate Matter on Visibility." Since the meteorological effects, as well as reduction of visibility, are considered in detail in the above document, only the salient features of this problem are summarized here.

Visibility in the atmosphere is reduced by the scatter and absorption of visible radiation by aerosols. Attenuation by scatter and absorption of the light passing from objects to observer reduces the brightness and contrast between objects with the result that the eye's ability to distinguish objects from their background is reduced.

In addition to reducing visibility by attenuation, aerosols that scatter light efficiently are effective in reducing object contrast and visibility because they also scatter light from the sky and sun into the line of sight of an observer.

It is a common observation that dark objects, for example mountain ridges, become progressively lighter in shade as they become more distant. The most distant mountain that one can distinguish is typically almost as light or bright as its sky background. Since particulate sulfur oxides are most effective in scattering light,[39] they represent air pollutants that play an important role in reducing visibility in the atmosphere.

The quantitative contribution made by the oxides of sulfur to the total scattering of light in various atmospheres has not been resolved, but sulfuric acid mist and other sulfate particulate matter are recognized as important sources of scattering. The latter arise, as noted earlier, from complex oxidation processes, some of which are photochemical in nature.

Although expressions for calculating visual range exist, dependent on particle size, number, refractive index, etc., they have limited usefulness because of the other scattering bodies which always accompany sulfur oxides in polluted atmospheres.[53-55]

H. SUMMARY

In 1965, an estimated 146 million tons of sulfur dioxide were emitted worldwide to the atmosphere, as compared to 78 million tons in 1940. The principal share, i.e., 70 percent, came from the combustion of coal, most of which was used to generate electrical power. The combustion and refining of petroleum products accounted for 18.9 percent of the total, while the remainder came from the smelting of sulfur-containing ores (10.8 percent). Papermaking and some other industrial operations also contributed minor amounts to the total.

In all of these processes, small amounts of sulfur trioxide or sulfuric acid are emitted also. Other oxides of sulfur are also emitted, but in quantities that are small by comparison; for example, about 40 to 80 parts of sulfur dioxide to one part of sulfur trioxide are emitted from fossil-fueled power plants. Sulfur dioxide is a nonflammable, nonexplosive, colorless gas that most people can taste at concentrations from 0.8 to 2.7 mg/m^3 (0.3 to 1 ppm) in air. At concentrations above 8.1 mg/m^3 (3 ppm) the gas has a pungent, irritating odor. In the atmosphere, sulfur dioxide, an acid anhydride, is partly converted to sulfur trioxide or to sulfuric acid and its salts by photochemical or catalytic processes. Sulfur trioxide is immediately converted to sulfuric acid in the presence of moisture. Laboratory and field investigations have shown that the oxidation of sulfur dioxide may proceed by several types of mechanism including (1) homogeneous gas phase reactions, (2) homogeneous catalysis in liquids, (3) heterogeneous gas-solid interactions, and (4) heterogeneous gas-liquid interactions. The predominant mechanism and the degree of oxidation are determined by a number of factors, including the concentration, the residence time in the atmosphere, the temperature, the humidity, the intensity and spectral distribution of incident radiation, and the presence of other pollutants such as metal oxides, hydrocarbons, and oxides of nitrogen.

Visibility in the atmosphere is reduced by the scatter and absorption of visible radiation by small particles in the size range from 0.1 to 1 micrometer in radius. This phenomenon is also described in Chapter 3 of a companion document, Air Quality Criteria for Particulate Matter.

The attenuation of light from an object and the illumination of the air between the object and the observer reduce the contrast of the object and hence reduce its visibility. Of the total suspended particulate matter in urban air, about 5 to 20 percent consists of sulfuric acid and other sulfates, and generally 80 percent or more of these particles by weight are smaller than 1 micrometer radius. Suspended sulfates in the air consequently are very effective in reducing visibility.

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Chapter 2

ATMOSPHERIC CONCENTRATIONS OF SULFUR OXIDES

A. INTRODUCTION

This chapter discusses the short and long-term measured concentrations of sulfur oxides in urban areas and in the vicinity of point sources such as power plants, refineries, and smelters. The relation of sulfur oxides in the atmosphere to the acidity of rainwater and of particulate matter also is reviewed.

B. ATMOSPHERIC CONCENTRATIONS OF SULFUR DIOXIDE

1. Concentrations in Urban Areas

Two major programs sponsored by the U.S. Public Health Service have provided the largest body of data on atmospheric sulfur dioxide concentrations in urban areas. For several years after its establishment, the Continuous Air Monitoring Project (CAMP) used the electroconductivity method for SO_2 determination in six large cities; more recently, CAMP has installed and is operating continuous, colorimetric SO_2 monitoring devices at all sites in addition to electroconductivity instruments. The National Air Surveillance Networks (NASN) use the colorimetric (West-Gaeke) method to provide 24-hour-sample data for about 200 locations on a 26-times-per-year basis. Recently, there has been a rapid expansion of State and local monitoring programs so that there are now several hundred active stations measuring ambient SO_2 levels across the United States. A few cities in the United States have installed systems which transmit data periodically to a central location where the data are processed.[1,2,3]

In Europe extensive monitoring networks have also been set up. In the Federal Republic of Germany, the North Rhine-Westphalia network covering about 5000 square kilometers began in 1964.[4,5,6] The Netherlands system telemeters concentrations of certain pollutants to a central station.[7] The English system covers the whole country.[8] The Japanese have extensive networks in many of their cities.[9,10] In Belgium 230 stations sample SO_2 and particulates automatically.[11] In Italy a network has been established through the main cities for which sampling and determinations are carried out by high school students.

Extensive monitoring programs yield large quantities of data which need to be reduced to a useful form. Maximum or average values alone do not provide a total picture of air quality. Distribution plots used in the U.S. show the percentage of the time sulfur dioxide concentrations are above certain levels. They give a more complete insight into the distribution of sulfur dioxide concentrations for a given site.

In the Federal Republic of Germany, where continuous monitoring stations are installed in most cities, another method of describing the immission load (ambient concentration) is used. Two important parameters of this method are the so-called immission indices I_1 and I_2.[12] Here I_1 is the confidence limit of arithmetic mean value and I_2 the 97.5 percent value of the sum-frequency distribution. Both of these parameters have the advantage that, contrary to the maximum value, they may be derived from any random sample. These statistics, for one year of observation, are given in Table 2-1.[5]

The frequency distributions obtained from CAMP measurements (for example, see Zimmer and Larsen[13]) show that sulfur dioxide concentrations are not symmetrically distributed but follow a log-normal distribution. This also has been established by Brasser, Joosting, and van Zuilen.[14] CAMP data are plotted as a frequency distribution for six

TABLE 2-1. SUMMARY OF SO_2 CONCENTRATION MEASUREMENTS IN THE FEDERAL REPUBLIC OF GERMANY, OCTOBER 1968-SEPTEMBER 1969 (EXCEPT IN NORDRHEIN-WESTFALEN AND KOLN WHERE THE PERIOD WAS NOVEMBER 1968-OCTOBER 1969). THE BASIC OBSERVATION WAS A 30-MINUTE AVERAGE CONCENTRATION.[5]

Station	Number of observations	Annual arithmetic average, mg/m^3	Maximum average		Concentrations not exceeded/exceeded by the indicated percentage of observations				
					not exceeded/exceeded				
			24 hours mg/m^3	30 minutes mg/m^3	50 percent mg/m^3	95 percent mg/m^3	0.2 percent mg/m^3	0.5 percent mg/m^3	1.0 percent mg/m^3
Baden-Württemberg									
Karlsruhe									
West	14 921	0,11	1,03	1,59	0,04	0,27	7,6	1,8	0,8
Kaiserallee	13 563	0,10	0,72	1,58	0,04	0,24	5,5	0,4	0,1
Mannheim									
Rheinau	11 911	0,12	0,71	1,59	0,05	0,26	9,2	2,7	0,7
Mitte	14 293	0,12	[illegible]	1,59	0,04	0,24	13,5	1,0	0,3
Bayern									
München									
Landshuter Allee	17 314	0,074	0,38	1,94	0,06	0,19	8,22	0,44	0.02
Müllerstr.	17 279	0,078	0,31	2,46	0.06	0,21	7.03	0,47	0,006
Krankenhaus Schwabing	17 036	0,056	0,32	0,76	0,05	0,18	5,55	0,33	0
Westendstr.	16 642	0,058	0,47	1,17	0,05	0,17	4,34	0,41	0.02
Bayerstr.	17 160	0,074	0,51	1,20	0,06	0,22	8,18	0,82	0.02
Pflugstr.	13 110	0,065	0,41	1,07	0,05	0,15	5,46	0,49	0,01
Aidenbachstr.	15 300	0,048	0,26	0,55	0,04	0,13	2,90	0,06	0
Hofmannstr.	13 734	0,058	0,27	0,63	0,05	0,16	2,54	0,12	0
Fernsehturm	11 114	0,064	0,25	0,64	0,04	0,19	5,58	0,16	0
Berlin									
Jungfernheide, Wasserwerk	16 134	0,152	0,67	1,50	0.11	0,45	26,04	3,68	0,20
Steglitz, Schloßstr.	16 802	0,152	0,82	1,28	0,15	0,45	33,94	3,56	0,21
Hamburg									
Innenstadt, Gorch-Fock-Wall	15 322	0,10	0,55	1,50	0,08	0,29	10,9	0,9	0,03
St. Pauli, Neuer Kamp	15 401	0,14	0,71	1,55	0,09	0,42	21,9	2,3	0.07
Steilshoop, Steilshooper Str.	12 223	0,09	0,50	1,40	0,07	0,35	15,6	1,3	0.02
Lohbrügge, Billwiese	12 250	0,08	0,47	1,04	0,04	0,27	8,3	0,7	0,02
Hessen									
Frankfurt									
Innenstadt, Feldbergstr.	16 152	0,130	0,48	0,85	0,09	0,34	23,0	0,6	0
West, Ackermannschule	16 313	0,121	0,53	1,00	0,09	0,34	16,5	1,1	0
Nahe Ostbahnhof	13 847	0,109	0,39	0,89	0,08	0,27	11,0	0,2	0
Kassel									
Ludwig-Mondstr.	8 455	0,090	0,32	1,06	0,03	0,25	6,8	0,6	0,05
Wiesbaden									
Victoriastr.	10 859	0,119	0,36	0,80	0,08	0,25	14,6	0,2	0

continued

TABLE 2-1 (cont.). SUMMARY OF SO_2 CONCENTRATION MEASUREMENTS IN THE FEDERAL REPUBLIC OF GERMANY, OCTOBER 1969-SEPTEMBER 1969 (EXCEPT IN NORDRHEIN-WESTFALEN AND KOLM WHERE THE PERIOD WAS NOVEMBER 1968-OCTOBER 1969). THE BASIC OBSERVATION WAS A 30-MINUTE AVERAGE CONCENTRATION.[5]

Station	Number of Observations	Annual arithmetic average, mg/m^3	Maximum average		Concentrations not exceeded/exceeded by the indicated percentage of observations				
					not exceeded		exceeded		
			24 hours mg/m^3	30 minutes mg/m^3	50 percent mg/m^3	95 percent mg/m^3	0.2 percent mg/m^3	0.5 percent mg/m^3	1.0 percent mg/m^3
Niedersachsen									
Salzgitter-Lebenstedt, Ostrand	15 664	0,096	0,71	1,66	0,05	0,34	11,5	1,1	0,13
Nordrhein-Westfalen									
Düsseldorf	7 764	0,105	0,46	1,04	0,07	0,26	9,90	0,65	0,01
Duisburg	8 336	0,160	0,96	1,64	0,12	0,45	25,23	3,87	0,37
Oberhausen	8 434	0,176	0,93	1,39	0,12	0,54	28,12	6,57	0,43
Bottrop	8 248	0,155	0,93	1,74	0,13	0,50	33,38	5,18	0,42
Essen-Mitte	8 440	0,147	0,89	1,49	0,12	0,37	22,22	2,25	0,19
Essen-Süd	8 040	0,105	0,60	1,29	0,08	0,30	17,26	1,13	0,07
Gelsenkirchen	8 455	0,169	0,85	1,44	0,13	0,46	31,21	4,08	0,22
Wanne-Eickel	7 629	0,138	0,77	1,29	0,11	0,35	22,51	2,94	0,10
Recklinghausen	8 289	0,147	0,60	1,09	0,12	0,34	24,60	1,15	0,07
Bochum	8 479	0,143	0,99	1,64	0,13	0,33	20,04	1,88	0,21
Castrop-Rauxel	8 097	0,158	0,53	1,04	0,11	0,37	29,08	1,67	0,02
Dortmund	7 410	0,131	0,93	1,39	0,11	0,32	18,43	1,69	0,19
Hagen	8 332	0,107	0,50	1,24	0,06	0,26	11,45	0,61	0,02
Köln									
Eifelwall	15 728	0,10	0,33	0,65	0,09	0,21	6,41	0,08	0
Buchforst	14 666	0,08	0,42	0,64	0,07	0,18	3,98	0,23	0
Ehrenfeld	15 868	0,09	0,29	0,81	0,08	0,19	4,35	0,13	0
Rheinland-Pfalz									
Ludwigshafen (Süd)	10 128	0,12	0,53	1,23	0,05	0,30	17,1	1,6	0,2
Saarland									
Völklingen, Feuerwehr	16 465	0,08	0,26	0,77	0,07	0,24	6,08	0,09	0

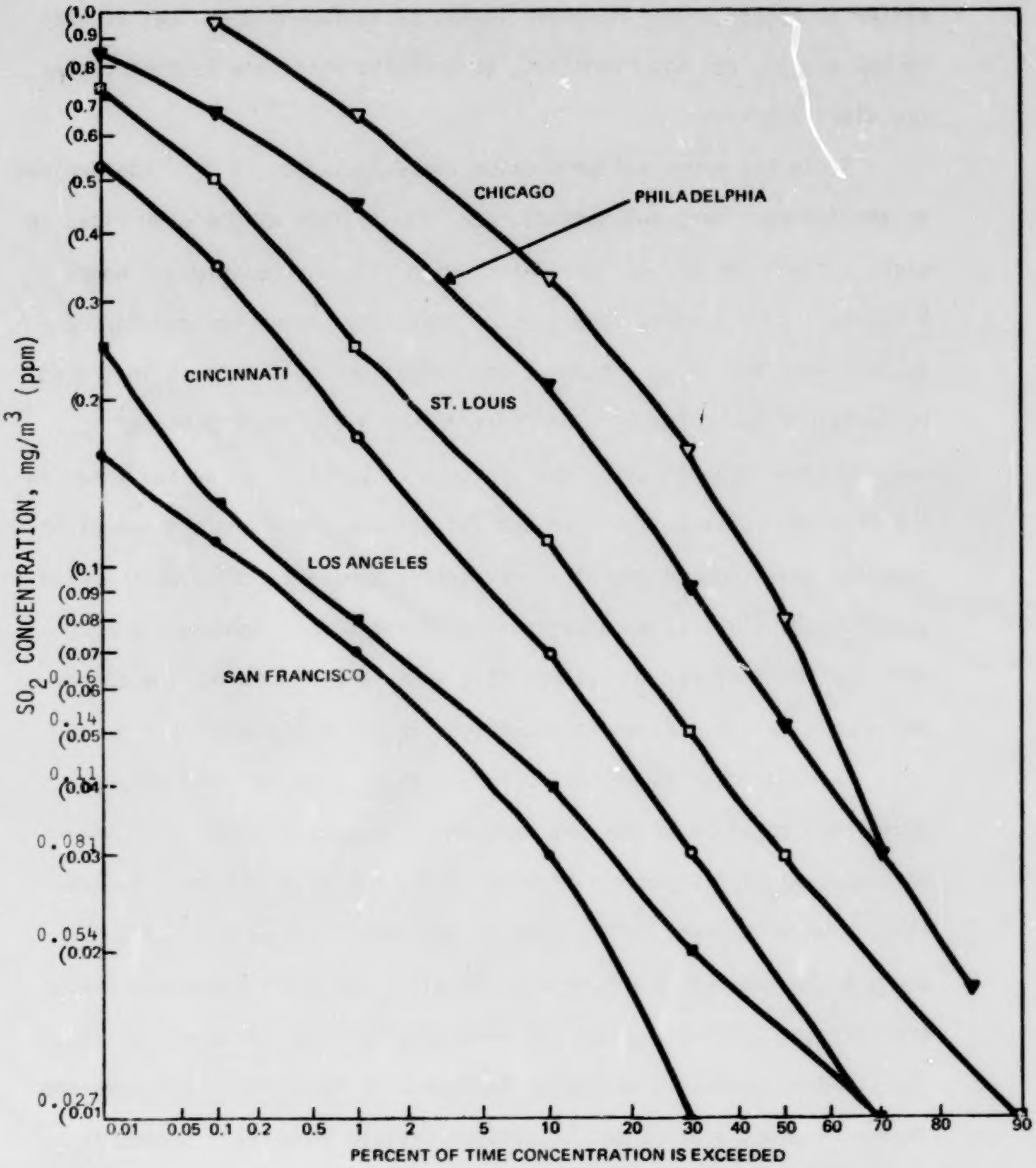

Figure 2-1. Frequency distribution of sulfur dioxide levels in selected American cities, 1962 to 1967 (1-hour averaging time, data from Table 2-2). (The approximate log normality of the distribution of sulfur dioxide concentrations is shown by the rather straight lines of the distribution functions when these are plotted on a logarithmic scale (concentrations) against a normal distribution frequency.)

cities in Figure 2-1. The lower levels of sulfur dioxide that prevail in Los Angeles and San Francisco, as compared with some Eastern cities, are clearly evident.

Table 2-2 gives sulfur dioxide concentrations, in g/m^3 (determined by the hydrogen peroxide method), for 1962 to 1967 at the CAMP sites in eight cities* for six different averaging times: 5 minutes, 1 hour, 8 hours, 1 day, 1 month, and 1 year. For some years, the monitoring systems were not in operation at some locations, and this is indicated by dashes in the columns. The first column gives the calculated maximum concentration using the approach of Larsen[15] described later in the chapter. Listed in the second and third columns are the geometric mean and the standard geometric deviation, similarly calculated, which describe the statistical distribution of the data. Columns 4 and 5 list the range of maximum values that were recorded during the 6-year period, while the maximum for each year is listed in columns 6 to 11.

From the data shown in Table 2-2, it is apparent that higher maxima are obtained as the averaging time becomes shorter. This is true because, for shorter averaging times, the instantaneous fluctuations have much greater influence on the resulting values. This is shown quite clearly in Figure 2-2, in which the maximum average concentrations are plotted against the averaging time for different cities. The standard geometric deviation (column 3 of Table 2-2) indicates the degree to which a given set of samples deviate from their geometric mean, and therefore it increases as the time period becomes shorter.

Data from the NASN stations, which cover more cities than the CAMP

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* There have been only six CAMP stations at any one time; their locations have changed through the years.

Table 2-2. CAMP DATA ON SULFUR DIOXIDE CONCENTRATIONS (ppm by volume)

City and averaging time	1962-1967					Maximum for year						Perct. data avail.
	Calc. annl. max.	Geo mean	SGD	Maxima								
				Max.	Min.	62	63	64	65	66	67	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	
Chicago:												
5 min	3.33	0.104	2.20	1.94	1.11	1.13	1.94	1.62	1.59	1.11	1.62	82
1 hr	1.60	0.111	2.01	1.69	0.86	0.86	1.69	1.12	1.14	0.98	1.11	82
8 hr	0.87	0.118	1.84	1.02	0.45	0.45	0.87	1.02	0.74	0.63	0.80	84
1 day	0.64	0.121	1.75	0.79	0.36	0.36	0.71	0.79	0.55	0.48	0.65	85
1 mo	0.24	0.133	1.44	0.35	0.13	0.18	0.33	0.35	0.27	0.27	0.32	93
1 yr	0.14	0.142	1.00	0.18	0.09	0.10	0.14	0.18	0.13	0.09	0.12	100
Cincinnati:												
5 min	1.85	0.016	2.94	1.15	0.65	0.84	0.99	0.88	1.15	0.70	0.65	82
1 hr	0.70	0.018	2.60	0.57	0.41	0.46	0.48	0.55	0.57	0.41	0.42	82
8 hr	0.31	0.020	2.31	0.38	0.14	0.14	0.23	0.27	0.38	0.18	0.18	83
1 day	0.21	0.021	2.16	0.18	0.10	0.11	0.11	0.14	0.18	0.10	0.13	83
1 mo	0.06	0.025	1.65	0.06	0.04	0.04	0.06	0.06	0.06	0.05	0.04	86
1 yr	0.03	0.029	1.00	0.04	0.02	0.03	0.03	0.04	0.03	0.03	0.02	100
Denver:												
5 min	0.36	0.013	2.11	0.96	0.33	.....	.....	.....	0.95	0.96	0.33	84
1 hr	0.18	0.014	1.94	0.36	0.17	.....	.....	.....	0.36	0.26	0.17	84
8 hr	0.10	0.015	1.79	0.14	0.05	.....	.....	.....	0.14	0.10	0.05	85
1 day	0.07	0.015	1.71	0.06	0.02	.....	.....	.....	0.06	0.05	0.02	86
1 mo	0.03	0.017	1.41	0.03	0.01	.....	.....	.....	0.03	0.02	0.01	92
1 yr	0.02	0.018	1.00	0.02	0.01	.....	.....	.....	0.02	0.01	.....	100
Los Angeles: *												
5 min	0.47	0.013	2.28	0.68	0.24	0.24	0.51	0.68	.....	.....	.....	59
1 hr	0.22	0.014	2.07	0.29	0.13	0.13	0.19	0.29	.....	.....	.....	67
8 hr	0.12	0.015	1.90	0.13	0.08	0.08	0.09	0.13	.....	.....	.....	71
1 day	0.09	0.015	1.80	0.10	0.06	0.06	0.07	0.10	.....	.....	.....	71
1 mo	0.03	0.017	1.46	0.03	0.02	0.03	0.03	0.02	.....	.....	.....	64
1 yr	0.02	0.018	1.00	0.02	0.02	0.02	0.02	.....	.....	.....	.....	67
Philadelphia:												
5 min	2.60	0.055	2.40	1.25	0.79	1.25	1.05	1.00	1.11	0.79	1.12	75
1 hr	1.16	0.060	2.17	1.03	0.66	1.03	0.85	0.84	0.94	0.66	0.77	76
8 hr	0.60	0.064	1.98	0.71	0.43	0.56	0.58	0.54	0.71	0.43	0.56	77
1 day	0.42	0.067	1.87	0.46	0.35	0.35	0.46	0.43	0.35	0.36	0.35	79
1 mo	0.15	0.075	1.50	0.15	0.12	0.13	0.12	0.15	0.13	0.13	0.13	86
1 yr	0.08	0.081	1.00	0.10	0.06	0.09	0.06	0.09	0.08	0.09	0.10	100
St. Louis:												
5 min	2.40	0.028	2.75	1.42	0.85	.....	.....	1.16	1.42	1.25	0.85	81
1 hr	0.96	0.031	2.45	0.96	0.55	.....	.....	0.73	0.96	0.84	0.55	81
8 hr	0.45	0.034	2.20	0.36	0.24	.....	.....	0.31	0.36	0.33	0.24	82
1 day	0.30	0.036	2.06	0.26	0.18	.....	.....	0.26	0.19	0.18	0.21	84
1 mo	0.09	0.042	1.60	0.08	0.05	.....	.....	0.08	0.06	0.06	0.05	88
1 yr	0.05	0.047	1.00	0.06	0.03	.....	.....	0.06	0.05	0.04	0.03	100
San Francisco:												
5 min	0.56	0.005	2.87	0.33	0.16	0.16	0.33	0.26	.....	.....	.....	64
1 hr	0.22	0.006	2.54	0.26	0.11	0.11	0.26	0.16	.....	.....	.....	64
8 hr	0.10	0.007	2.27	0.10	0.06	0.06	0.07	0.10	.....	.....	.....	65
1 day	0.07	0.007	2.12	0.08	0.05	0.05	0.05	0.08	.....	.....	.....	65
1 mo	0.02	0.008	1.63	0.03	0.01	0.01	0.02	0.03	.....	.....	.....	75
1 yr	0.01	0.010	1.00	0.02	0.01	.....	0.01	0.02	.....	.....	.....	67
Washington:												
5 min	1.19	0.039	2.17	0.87	0.42	0.42	0.56	0.87	0.44	0.47	0.44	69
1 hr	0.58	0.042	1.99	0.62	0.35	0.38	0.48	0.62	0.35	0.45	0.37	69
8 hr	0.32	0.044	1.83	0.35	0.22	0.23	0.35	0.32	0.27	0.34	0.22	70
1 day	0.23	0.046	1.74	0.25	0.15	0.18	0.25	0.22	0.20	0.25	0.15	71
1 mo	0.09	0.050	1.43	0.11	0.07	0.10	0.11	0.09	0.08	0.10	0.07	75
1 yr	0.05	0.050	1.00	0.05	0.04	0.05	0.05	0.04	0.05	0.04	.....	83

*See footnote on page 2-8.

Table 2-2 (cont.). CAMP DATA ON SULFUR DIOXIDE CONCENTRATIONS (ppm by vol.)

City and averaging time	Percent of time concentration is exceeded								
	.001	0.01	0.1	1	10	30	50	70	90
	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)
Chicago:									
5 min	1.75	1.34	1.03	0.68	0.33	0.16	0.08	0.03	0.01
1 hr	-------	1.12	0.96	0.65	0.33	0.16	0.08	0.03	0.01
8 hr	-------	-------	0.76	0.57	0.32	0.16	0.09	0.04	0.01
1 day	-------	-------	-------	0.50	0.31	0.16	0.09	0.05	0.02
1 mo	-------	-------	-------	-------	0.27	0.17	0.09	0.06	0.03
1 yr	-------	-------	-------	-------	-------	-------	0.12	-------	-------
Cincinnati:									
5 min	0.90	0.70	0.42	0.19	0.07	0.03	0.02	0.01	0.00
1 hr	-------	0.53	0.35	0.17	0.07	0.03	0.02	0.01	0.00
8 hr	-------	-------	0.22	0.12	0.06	0.04	0.02	0.02	0.01
1 day	-------	-------	-------	0.10	0.06	0.04	0.03	0.02	0.01
1 mo	-------	-------	-------	-------	0.05	0.04	0.03	0.02	0.01
1 yr	-------	-------	-------	-------	-------	-------	0.03	-------	-------
Denver:									
5 min	0.64	0.33	0.18	0.07	0.03	0.01	0.01	0.00	0.00
1 hr	-------	0.26	0.11	0.06	0.03	0.02	0.01	0.00	0.00
8 hr	-------	-------	0.08	0.04	0.03	0.02	0.01	0.00	0.00
1 day	-------	-------	-------	0.04	0.03	0.02	0.01	0.00	0.00
1 mo	-------	-------	-------	-------	0.02	0.02	0.01	0.01	0.00
1 yr	-------	-------	-------	-------	-------	-------	0.01	-------	-------
Los Angeles: *									
5 min	0.56	0.38	0.15	0.08	0.04	0.02	0.01	0.01	0.00
1 hr	-------	0.25	0.13	0.08	0.04	0.02	0.01	0.01	0.00
8 hr	-------	-------	0.10	0.07	0.04	0.02	0.02	0.01	0.00
1 day	-------	-------	-------	0.06	0.04	0.02	0.02	0.01	0.00
1 mo	-------	-------	-------	-------	0.02	0.02	0.02	0.01	0.01
1 yr	-------	-------	-------	-------	-------	-------	0.02	-------	-------
Philadelphia:									
5 min	1.18	0.95	0.72	0.47	0.21	0.09	0.05	0.03	0.01
1 hr	-------	0.85	0.66	0.45	0.21	0.09	0.05	0.03	0.01
8 hr	-------	-------	0.49	0.37	0.19	0.10	0.06	0.04	0.01
1 day	-------	-------	-------	0.29	0.18	0.10	0.07	0.04	0.02
1 mo	-------	-------	-------	-------	0.12	0.10	0.08	0.07	0.03
1 yr	-------	-------	-------	-------	-------	-------	0.09	-------	-------
St. Louis:									
5 min	1.23	0.96	0.58	0.29	0.11	0.05	0.02	0.01	0.00
1 hr	-------	0.73	0.50	0.25	0.11	0.05	0.03	0.01	0.00
8 hr	-------	-------	0.29	0.19	0.09	0.06	0.04	0.02	0.00
1 day	-------	-------	-------	0.14	0.09	0.05	0.04	0.02	0.01
1 mo	-------	-------	-------	-------	0.06	0.05	0.04	0.03	0.02
1 yr	-------	-------	-------	-------	-------	-------	0.04	-------	-------
San Francisco:									
5 min	0.30	0.18	0.13	0.07	0.03	0.01	0.01	0.00	0.00
1 hr	-------	0.16	0.11	0.07	0.03	0.01	0.01	0.00	0.00
8 hr	-------	-------	0.09	0.06	0.03	0.02	0.01	0.00	0.00
1 day	-------	-------	-------	0.05	0.03	0.02	0.01	0.00	0.00
1 mo	-------	-------	-------	-------	0.02	0.01	0.01	0.01	0.00
1 yr	-------	-------	-------	-------	-------	-------	0.01	-------	-------
Washington:									
5 min	0.65	0.49	0.36	0.22	0.11	0.06	0.03	0.02	0.01
1 hr	-------	0.46	0.35	0.21	0.10	0.06	0.03	0.02	0.01
8 hr	-------	-------	0.26	0.19	0.10	0.06	0.04	0.02	0.01
1 day	-------	-------	-------	0.17	0.10	0.06	0.04	0.02	0.01
1 mo	-------	-------	-------	-------	0.09	0.05	0.04	0.03	0.02
1 yr	-------	-------	-------	-------	-------	-------	0.04	-------	-------

*Los Angeles was not a CAMP Station; data was supplied by the Los Angeles County Air Pollution Control District.

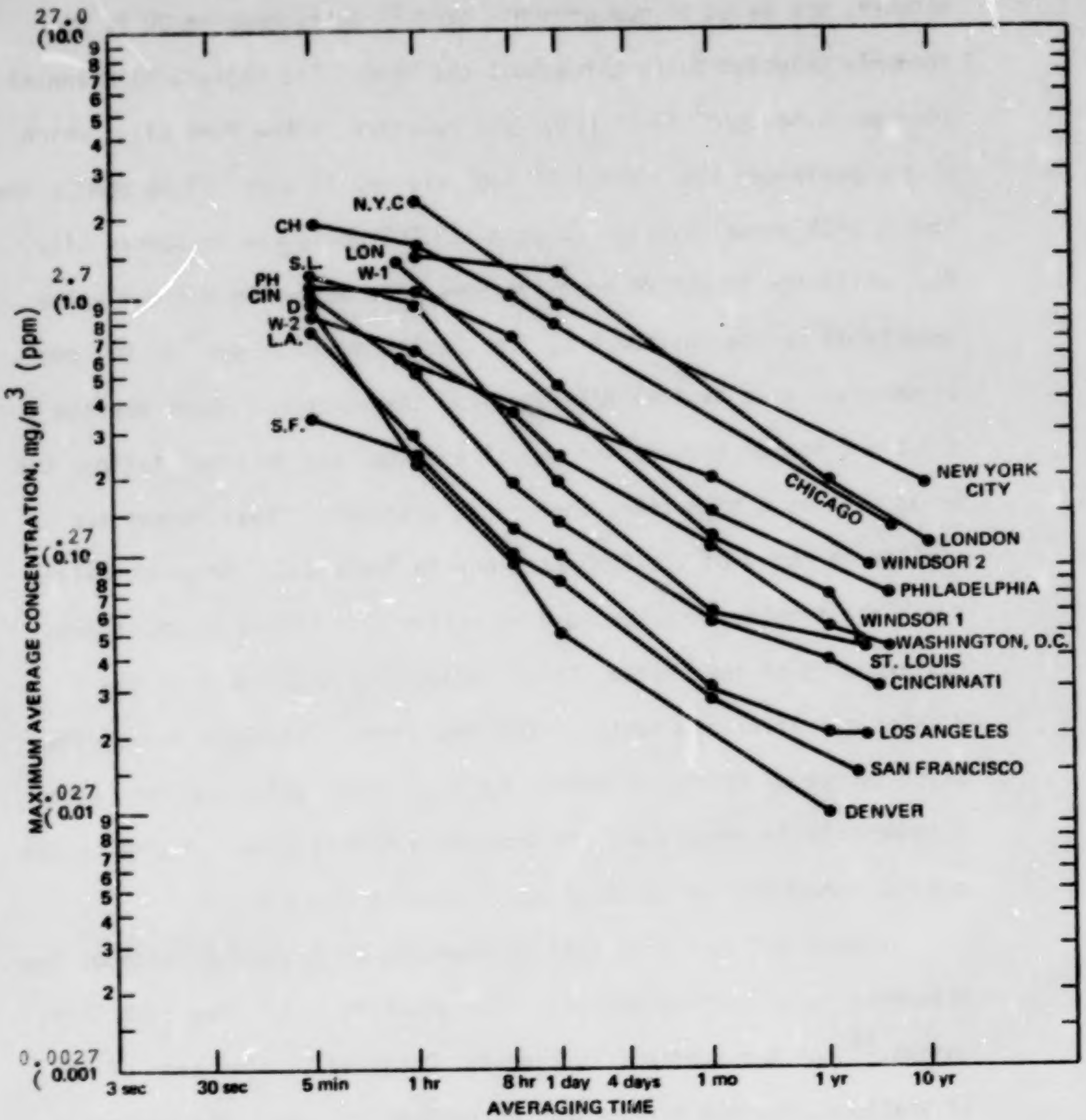


Figure 2-2. Long-time average sulfur dioxide concentrations (mg/m^3 (ppm)) and associated maximum average concentrations for various time periods for twelve sites in eleven cities. (For each of the given lines, the last point on the right is the long-term average over the interval specified, while the other points represent the maxima within the interval for the averaging periods shown. If, for example, one complete year of data were available, in terms of hourly averages, there would be one maximum hourly value for that year. If five years of data were available, in terms of hourly averages, five maxima (one for each year) would be obtained, and the highest of these five maxima would constitute the maximum hourly average for the five-year period.)

network, are based on measurements over 24 hours made on 20 to 26 randomly selected dates throughout the year. The highest NASN annual average (0.46 mg/m^3 (0.17 ppm)) was recorded in New York City, which also experienced the highest 24-hour average (1 mg/m^3 (0.38 ppm)); the lowest NASN annual average (5 µg/m^3 (0.002 ppm)) was in Kansas City, Mo., while the lowest 24-hour averages were below the minimum value detectable by the instruments, i.e., below about 3 µg/m^3 (0.001 ppm). In general, at a typical NASN station, the maximum 24-hour average is about 3 times as high as the annual average, but at some stations can be as high as 6 to 8 times the annual averages. These ranges are similar to those of the CAMP stations in Table 2-2. Geographically, the highest values are recorded at stations in cities in the northeastern part of the United States, especially those east of the Mississippi River and north of the Ohio River. In these areas, the major source of energy is fossil fuels of high sulfur content, such as domestically-mined coal and imported residual oils. Maxima in the diurnal concentration curve usually occur at about 8 a.m.

Figure 2-2 is a graphical counterpart of Table 2-2, without the frequency distributions but with four stations added (New York City, London,[16] and two stations in Windsor, Ontario).[17] For each of the 12 stations, maximum average concentrations are shown for various averaging times. Since the averaging times are not comparable in some cases, the time points for which maxima are available have been connected in order to approximate the relationship between the corresponding maxima. As expected, a station with a relatively high maximum concentration for one averaging time is likely to show, in proportion, an equally high maximum concentration for other averaging times. A station with a low maximum concentration for one averaging time likewise shows an equally low maximum concentration for other averaging times.

The last nine columns of Table 2-2 give the frequency distribution of concentrations for each of these averaging times (or subsets of these values; for example, for 1 year, with at most six measurements available, only the median, or 50-percentile concentration, is given). While the maximum of columns 6 to 11 were tabulated on a year-by-year basis, the frequency data shown here (columns 12 through 20) are applicable to the entire 6-year period. The value listed in a given column is the concentration which is exceeded the stated percentage of the time.

The 30-percentile point (which is very close to the arithmetic mean) apparently represents an equilibrium condition, since the concentration associated with this point is approximately the same for all averaging times. Thus, the 30-percentile concentration, i.e., the value which is not exceeded for 70 percent of the time, might be used as a simple indicator of the "general sulfur dioxide level" of a city, irrespective of the averaging time. For the eight cities tabulated, using this index, Chicago clearly shows the highest level (0.4 mg/m^3 (0.16 ppm)), followed by Philadelphia, Washington, St. Louis, Cincinnati, Los Angeles, Denver, and San Francisco. That this is a good index is borne out by Figure 2-3, which shows the annual average sulfur dioxide concentrations, by year, for these same cities. The ordering of the cities, from most severe to least severe, appears to be the same, with Chicago on the top and San Francisco on the bottom.

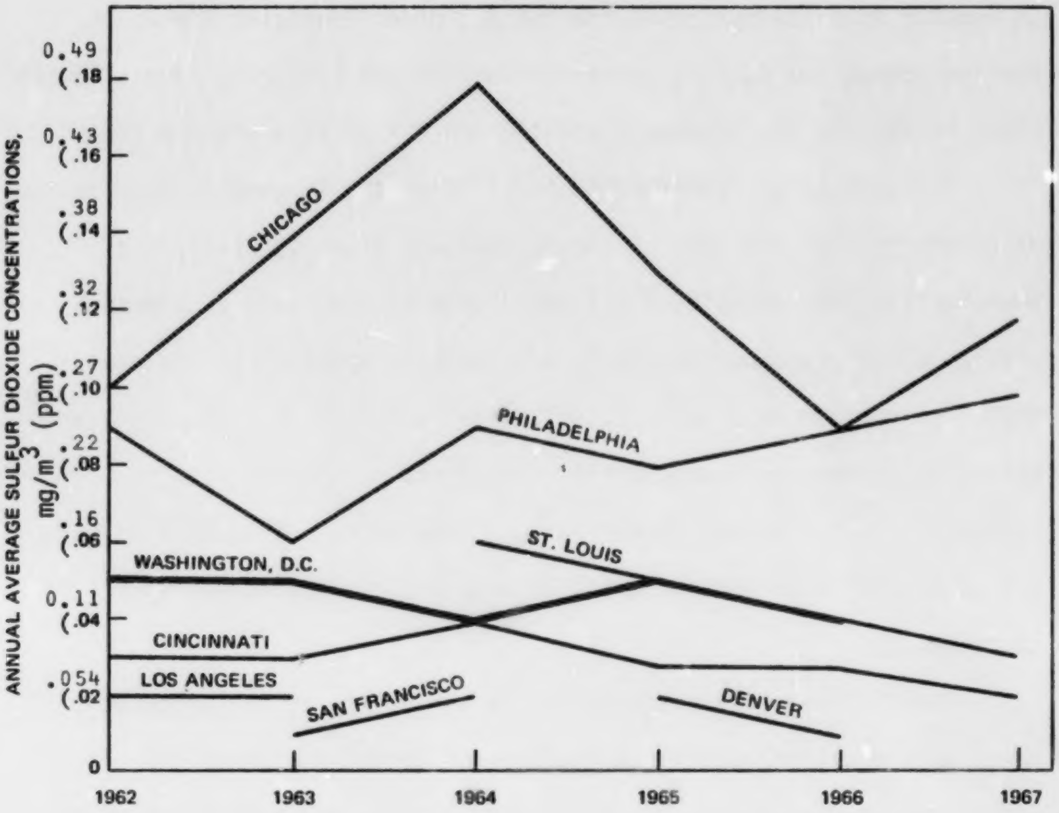


Figure 2-3. Trends in sulfur dioxide concentration for eight cities. (This figure shows that the sulfur dioxide concentrations for the years 1962-1967 were highest in Chicago and Philadelphia; sampling periods begin on December 1 of the preceding year and run until November 30 of the year shown.)

The conversion of the maximum concentration for one averaging time to that for another may be approached in a number of ways. Brasser, Joosting, and van Zuilen[14], in a manner similar to that described above, attempt to establish empirically the relationship between maxima for different averaging times from measurements carried out over long periods and under different meteorological conditions.

Larsen[15] computes the expected maximum concentration (C) for a given averaging time by using the geometric mean (M_g), the standard geometric deviation (σ_g), and the "standard normal deviate" of no more than one occurrence in 1.67N trials (z). His formula is

$$C = M_g \sigma_g^{\,z} \qquad (2\text{-}1)$$

For example, if data for 1 year are available, if the 1-hour geometric mean concentration is 0.12 mg/m^3 (0.044 ppm), and if the 1-hour standard geometric deviation is 2.46, then the calculated maximum hourly concentration, expected to occur about once a year is

$C_{max(hour)}$ = 0.12 mg/m^3 (0.044 ppm) $(2.46)^{3.81}$ = 3.7 mg/m^3 (1.36 ppm),

since there are 8,760 hours in a year and the standard normal deviate corresponding to a probability of $\frac{1}{(8760)\ (1.67)}$ (or 0.0000685) is 3.81. Likewise, if M_g and σ_g are unchanged but the total period of observation is only 26 hours, then, since the standard normal deviate corresponding to a probability of $\frac{1}{(26)\ (1.67)}$ or (0.0231) is 1.99,

$C_{max(hour)}$ = 0.12 mg/m^3 (0.044 ppm) $(2.46)^{1.99}$ = 0.73 mg/m^3 (0.27 ppm).

Or, in other words, this hourly average concentration is expected to be exceeded about once a day.

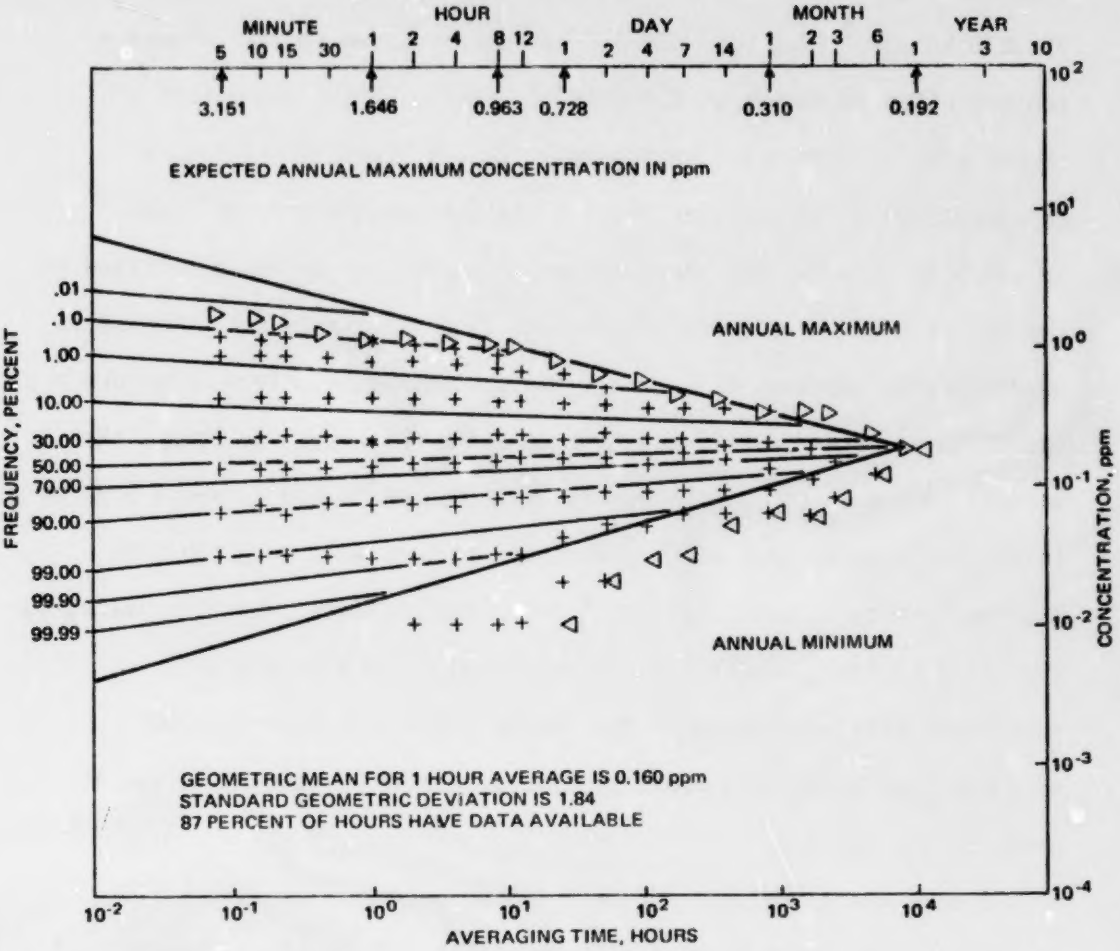
In a similar manner, it is possible also to calculate the minimum concentration for a given averaging time, as well as the concentrations at various percentiles, using the geometric mean and the standard geometric deviation for that averaging time. In addition, the geometric mean and the standard geometric deviation for one averaging time can be calculated from data obtained for other averaging times, although the accuracy of the results will depend on the number of air samples taken compared to the total number of samples that could have been taken if air sampling had been continuous. A set of 22 24-hour-duration random values were selected from the CAMP data by use of an NASN sampling schedule and were analyzed by Zimmer and Larsen.[13] For the 1-hour-averaging values, these investigators calculated a geometric mean of 0.15, as compared with 0.14, and a standard geometric deviation of 1.76, as compared with 1.94. Thus, a fairly good approximation of the year's hourly average frequency distribution could have been obtained with these 22 random samples.

Maxima calculated by Larsen's method are reasonable for averaging times of 1 hour or greater but tend to give overestimates for 5-minute periods; they do so for six of the eight cities in Table 2-2 (first column). The lower measured values may be partially due to the response times of the instruments. Table 2-3 compares the calculated maximum concentrations for six averaging times for the period from December 1, 1963, to December 1, 1964, with those actually observed in Chicago during the calendar year 1964. It is seen that the calculated

Table 2-3. COMPARISON OF CALCULATED AND OBSERVED MAXIMUMUM SULFUR DIOXIDE CONCENTRATIONS FOR VARIOUS AVERAGING TIMES in 1964 IN CHICAGO

Averaging time	Predicted maximum, mg/m^3	Observed maximum, mg/m^3
5 minutes	8.5	4.4
1 hour	4.4	3.0
8 hours	2.6	2.8
1 day	2.0	2.1
1 month	0.84	0.95
1 year	0.52	0.49

value for averaging times as short as 5 minutes deviates markedly from the observed value. A plot of sulfur dioxide concentration data for Chicago from December 1, 1963, to December 1, 1964, is given in Figure 2-4. Averaging time is on a logarithmic scale, as is



GEOMETRIC MEAN FOR 1 HOUR AVERAGE IS 0.160 ppm
STANDARD GEOMETRIC DEVIATION IS 1.84
87 PERCENT OF HOURS HAVE DATA AVAILABLE

Figure 2-4. Concentration of sulfur dioxide in Chicago for various averaging times and frequencies, from December 1, 1963 to December 1, 1964. (For brief intervals, the concentration reached values as high as 2.7 mg/m^3 (1 ppm) or 5.4 mg/m^3 (2 ppm), but for increasing averaging times, the upper and lower limits converge to a value near 0.54 mg/m^3 (0.2 ppm).)

concentration in g/m^3, while frequency (percent) is given on a normal probability scale. The crosses and triangles in the figure denote observed values, while the lines represent calculated concentrations. For example, for an averaging time of 1 hour, 30 percent of the 1-hour-duration samples obtained during the year exceeded a concentration of about 0.54 mg/m^3 (0.2 ppm) and 0.1 percent of these samples showed a concentration in excess of 2.7 mg/m^3 (1 ppm). (These two points are marked with asterisks in the figure.) The 13 lines in the figure represent the 11 percentiles and the maximum and the minimum lines. In addition, several expected maximum concentration values are listed at the top of the figure. Thus the middle line represents the expected 50 percentile (or median) line, i.e., the concentration values which one would expect to be exceeded half the time at different averaging times. For example, for a 1-hour averaging time this concentration is about 0.32 mg/m^3 (0.12 ppm). At several points, percentile lines will coincide with maximum or minimum concentration lines. For instance, when the averaging time is 0.88 hour and the total time period is 1 year, the 0.01 percentile will correspond to the maximum, since there are 10,000 of these time-units in a year; similarly, the 99.99 percentile corresponds to the minimum.

A more exact analysis of the relation between statistical parameters like maximum value or percentiles and the underlying averaging time has to follow the principles of spectral analysis. According to this theory the variance as a basic value is related to the averaging time in the following way:

$$s^2 (\bar{c}_k) = \frac{s^2 (\bar{c}_1)}{k} \left[1 + 2 \sum_{r=1}^{k-1} \frac{k - r}{k} \; ac\,(r) \right] \qquad (2\text{-}2)$$

where s^2 (c_1) is the variance pertaining to the averaging time Δt, s^2 ($\bar{c}_k$) is the variance pertaining to the k-multiple of Δt. ac (r) is the autocorrelation of the time lag k in units of Δt. Other parameters like percentiles (p) or maximum values (m) are at least approximately proportional to the standard deviation s:

$$m_k = \alpha \; s \; (\bar{c}_k) \tag{2-3}$$

$$\text{or} \quad p_k = \beta \; s \; (\bar{c}_k) \; . \tag{2-4}$$

The coefficients α and β can be derived from setting the index k in the above mentioned functions equal to 1 and calculating m and p for Δt.

An example of an autocorrelation function based on five years of data from an SO_2-monitoring station in Düsseldorf is shown in Figure 2-5.[18] The calculated standard deviation compared with empirical results is shown in Figure 2-6. Figure 2-7 shows that the periodicity of the day is of significant influence on the autocorrelation and consequently on the standard deviation. This may also explain the deviation between model and reality in Figure 2-6. The graph of the spectral density P* (f) in Figure 2-7 shows that three such periodicities exist, namely for 8, 12, and 24 hours.

2. Concentrations Related to Point Sources

An industrial plant which emits large quantities of sulfur dioxide is described as a point source. The area near such sources may experience high concentrations or immeasurably small values, depending on the prevailing winds, throughput differences, intermittent operations, intermittent pressure releases, and differences in velocity and temperature of emissions. Several studies of such situations have been reported.[19,20]

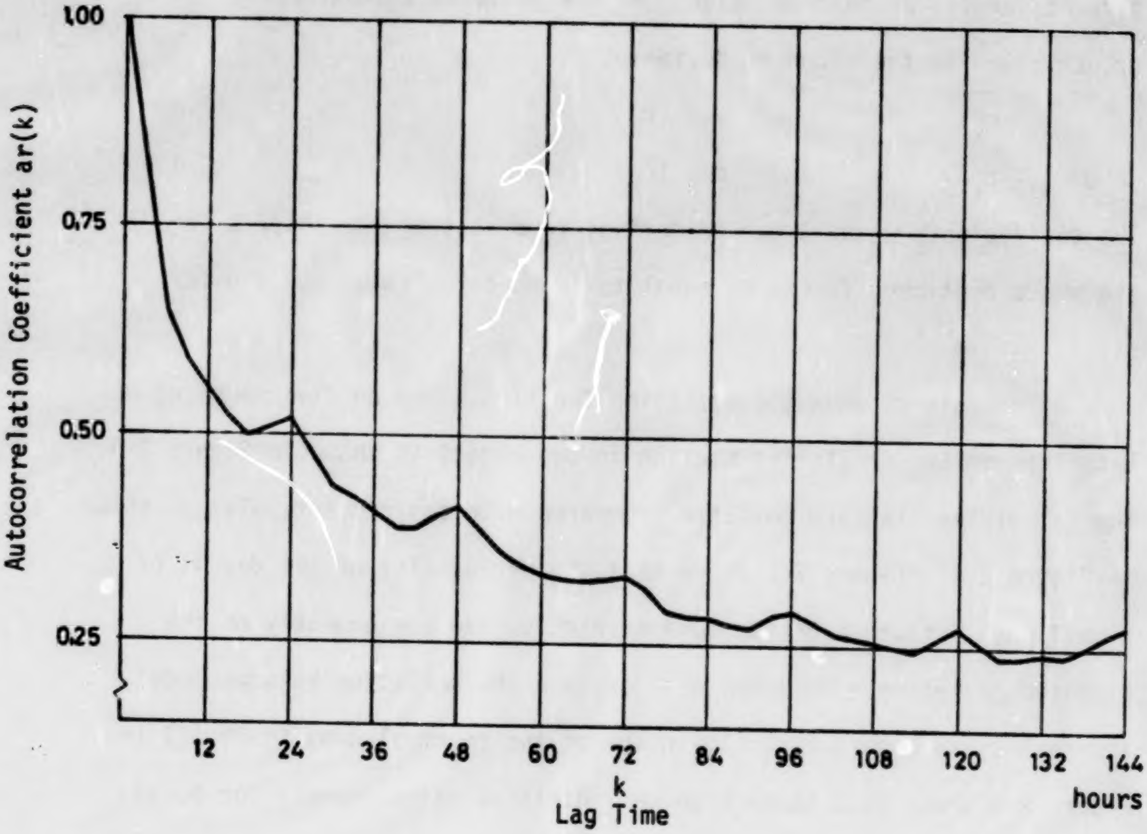


Figure 2-5. The autocorrelation coefficient ar(k) as a function of lag time k. Based on five years of data from an SO_2-monitoring station in Düsseldorf.[18]

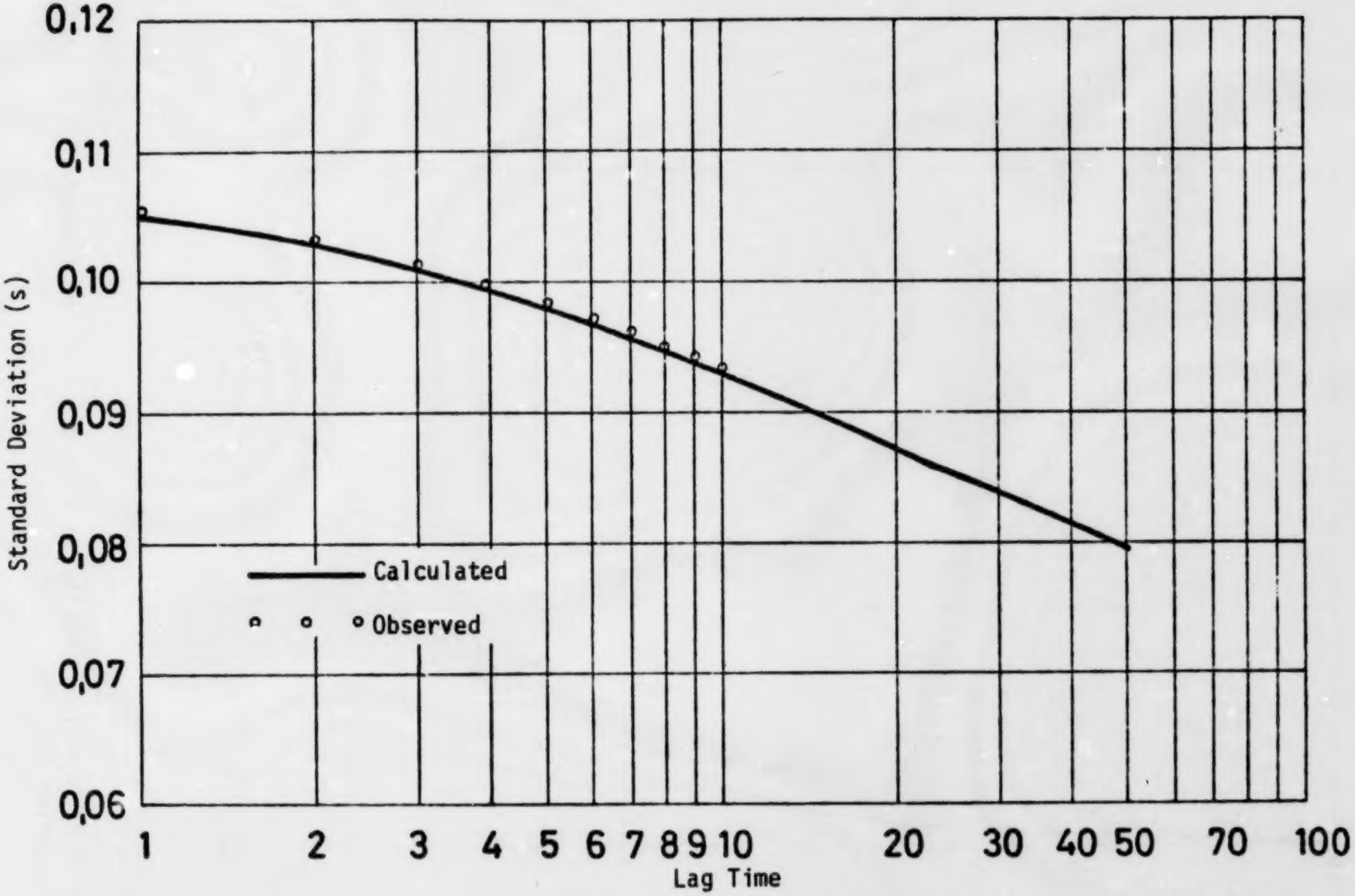


Figure 2-6. Standard deviation derived from the autocorrelation of SO_2 measurements.

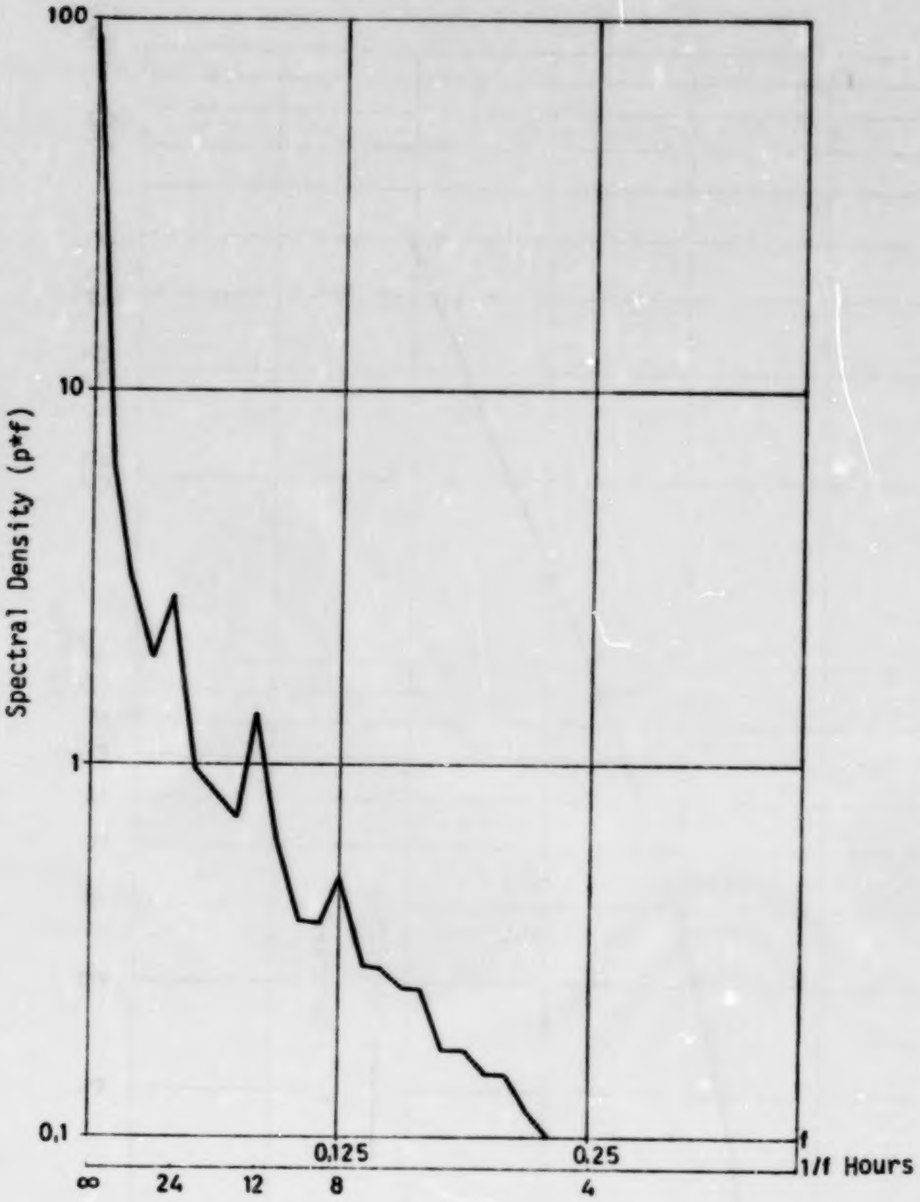


Figure 2-7. Spectral density as a function of the frequency f as well as the period 1/f.

a. Copper Smelter, Australia, 1962

Sullivan[21] reported that the maximum daily average concentrations were from 8 to 17 times the annual average concentration. At a station located 2.4 kilometers from the smelter, the hydrogen peroxide method gave a maximum daily average of 1.6 mg/m^3 (0.60 ppm), while the annual average was 0.097 mg/m^3 (0.036 ppm). A Thomas Autometer (conductometric) indicated peak concentrations from 2.7 to 13.5 mg/m^3 (1 to 5 ppm) on 30 occasions during a 6-month period and a maximum peak of 36.5 mg/m^3 (13.5 ppm).

b. Oil Refinery, 1965

Concentrations in excess of 1.4 mg/m^3 (0.5 ppm) for 10 hours during 1 month with momentary peaks over 5.4 mg/m^3 (2 ppm) in an area near an oil refinery were reported by Linzon.[22]

c. Smelter, Canada, 1958

A station located 13 kilometers from a smelter recorded an average concentration of 0.08 mg/m^3 (0.03 ppm) during a 4-month study (May-August 1958). Measurable concentrations were present about 20 percent of the time, and concentrations above 0.68 mg/m^3 (0.25 ppm) occurred 4 percent of the time.[23]

d. Smelter, Trail, Canada, 1931 to 1937

During the 6-month growing season, a station 24 kilometers south of the smelter recorded these data:

	1931	1932	1933	1934	1935	1936	1937
Average SO_2, mg/m^3	0.086	0.019	0.022	0.032	0.062	0.060	0.035
Hours with $SO_2 > 0.68$ mg/m^3	140	8.5	18	32.5	36	47	7

The concentrations are 6-month averages and the hours during which more than 0.68 mg/m^3 (0.25 ppm) of sulfur dioxide was measured constitute from 0.2 to 3.5 percent of the total time. Maximum concentrations that lasted from 4 to 54 minutes ranged from 1.3 to 3.5 mg/m^3 (0.48 to 1.3 ppm) or from 30 to 160 times the respective 6-month averages.[20] The latter represents a considerably higher ratio than those which can be calculated from Table 2-2 and demonstrates the impact of point sources versus multiple sources.

e. Power Plant, 1966

Sulfur dioxide from a 1,000-megawatt power station burning 430 tons of 1.5 percent sulfur coal per hour was studied by Martin and Barber.[24] Sixteen sulfur dioxide recorders were spaced around a ring of radius about 4.8 to 6.4 kilometers centered on the station, i.e., near the zone of calculated maximum ground-level pollution. The maximum 3-minute concentration during the year was about 1.7 mg/m^3 (0.62 ppm), the maximum hourly average was about 1.3 mg/m^3 (0.47 ppm), the maximum daily average was 0.30 mg/m^3 (0.11 ppm), and the annual average was about 0.073 mg/m^3 (0.027 ppm).

f. Power Plant, Pennsylvania, 1961

A second study of sulfur dioxide concentrations near a coal-fired power plant was made by McCaldin and Bye.[25] A Thomas Autometer 0.8 kilometer from this plant indicated an average concentration of 0.46 mg/m^3 (0.17 ppm) from January to April (0.24 mg/m^3 (0.09 ppm) by colorimetric West-Gaeke) with a maximum hourly average of 7.9 mg/m^3 (2.9 ppm) and a momentary peak concentration of 12.7 mg/m^3 (4.7 ppm).

C. SULFURIC ACID AND ITS RELATION TO SULFUR DIOXIDE

Measurements of sulfuric acid along with sulfur dioxide estimations are of interest because of the higher irritant potential of sulfuric acid, and because the ratio of the concentrations of the two pollutants found under various conditions helps in our understanding of the mechanism of the oxidation of sulfur dioxide to sulfuric acid in the atmosphere.

Coste[26] and Coste and Courtier[27] in 1935 made simultaneous measurements of sulfuric acid and sulfur dioxide in London, England. Sulfur dioxide concentrations ranged from 371 to 1657 $\mu g/m^3$ (0.13 to 0.58 ppm); sulfuric acid concentrations ranged from 4 to 20 $\mu g/m^3$. The weight ratio of sulfuric acid to sulfur dioxide was 0.011 at the higher concentration of sulfur dioxide and 0.013 at the lower concentration. The highest ratio of sulfuric acid to sulfur dioxide was 0.023 on a misty day.

A maximum sulfur dioxide concentration of 4200 $\mu g/m^3$ (1.47 ppm) in London during the period December 2 through December 5, 1957, was reported by Commins.[28] During the same period the maximum concentration of sulfuric acid was 222 $\mu g/m^3$. The ratio of maximum sulfuric acid to maximum sulfur dioxide was 0.053. Commins also reported that sulfuric acid could be as much as 10 percent of the total sulfur corresponding to a weight ratio of sulfuric acid to sulfur dioxide of 0.167.

An extensive study of the simultaneous presence of sulfur dioxide and sulfuric acid mist in the air was made by Bushtueva.[29,30] Between August 1953 and January 1954, she collected 198 paired samples for sulfur dioxide and sulfuric acid determination. The data are presented in Table 2-4. (The concentrations of sulfur dioxide in ppm have been added for convenience of comparison with other data reported in ppm.) These data show that as the sulfur dioxide concentration increases so does the sulfuric acid concentration, although at a slower rate.

Table 2-4. CONCENTRATION OF SULFUR DIOXIDE AND SULFURIC ACID MIST OBSERVED IN AIR[29,30]

SO_2 concentrations		Number of tests	Average concentration			H_2SO_4 : SO_2 Weight ratio
			SO_2		H_2SO_4	
$\mu g/m^3$	ppm		ppm	$\mu g/m^3$	$\mu g/m^3$	
24-hour samples:						
25–100	0.009–0.035	6	0.01	30	12.6	0.420
101–250	0.035–0.088	18	0.06	176	19.6	0.112
251–500	0.088–0.175	38	0.14	387	20.0	0.051
501–750	0.176–0.263	20	0.23	663	31.0	0.045
751–1000	0.264–0.350	6	0.30	866	29.0	0.033
Over 1000	over 0.35	11	0.43	1220	43.0	0.035
Single samples:						
Up to 250	up to 0.088	15	0.05	128	17.5	0.137
251–750	0.088–0.263	3	0.15	428	41.6	0.097
Over 750	over 0.263	2	0.48	1380	326.0	0.235

Bushtueva also studied the effect of wind speed and relative humidity on the concentrations of sulfur dioxide and sulfuric acid. Both the sulfuric acid concentration and the ratio of sulfuric acid to sulfur dioxide were highest during periods of fog, and lowest during periods of precipitation. In the absence of precipitation, the ratio of sulfuric acid to sulfur dioxide increased from about 0.045 at 60 percent relative humidity to about 0.090 at 90 percent relative humidity, and to 0.15 at relative humidities above 91 percent. At wind speeds below about 2.0 m/sec., the ratio of sulfuric acid to sulfur dioxide was 0.173, and at wind speeds greater than about 4.0 m/sec. the ratio was only 0.068. Thus calm days, high humidity, and especially foggy weather are associated with high concentrations of sulfuric acid.

Although they did not study the relation of sulfuric acid to sulfur dioxide, Mader et al.[31] found that the sulfuric acid concentration at Los Angeles increased as the relative humidity increased.

Chaney[32] studied the relationship between sulfur dioxide (West-Gaeke measurement) and sulfuric acid in the Los Angeles area. During the time of the study, sulfur dioxide values were generally very low and sometimes there was no measurable sulfate. The weight ratios of sulfuric acid to sulfur dioxide ranged from 0.037 to 3.0 and the sulfate levels were relatively high compared to the sulfur dioxide concentrations. The data of the National Air Surveillance Network also indicate a large amount of sulfate per unit of sulfur dioxide as measured by the West-Gaeke technique. In the strongly oxidizing atmosphere of Los Angeles, sulfur dioxide may be rather rapidly oxidized. On the other hand, the high ozone and nitrogen dioxide concentrations in Los Angeles may significantly interfere with the West-Gaeke procedure so that if the sulfamic acid modification is not used, values lower than actual sulfur dioxide concentrations may be recorded; consequently oxidation of sulfur dioxide may be more apparent than real.

Thomas[33] used an automatic electroconductivity measuring instrument for the simultaneous measurement of sulfur dioxide and sulfuric acid mist concentrations during the winter of 1961 in Los Angeles. Concentrations of sulfur dioxide up to 600 $\mu g/m^3$ (0.21 ppm) and of sulfuric acid up to 50 $\mu g/m^3$ were observed (Table 2-5). The weight ratios of sulfuric acid to sulfur dioxide lie between 0.032 and 0.246; these ratios are within the range of values reported by other investigators for other places.

Thomas' data indicate a nonlinear relationship between sulfur dioxide and sulfuric acid concentrations. Sulfuric acid increases as sulfur dioxide increases up to some critical value, depending upon the location. Beyond the critical value, sulfuric acid decreases as sulfur

Table 2-5. CONCENTRATIONS OF SULFUR DIOXIDE AND SULFURIC ACID MIST OBSERVED IN 1961 IN AIR OVER LOS ANGELES AND ONE OF ITS SUBURBS, EL SEGUNDO[33]

Date	Sulfur dioxide		Sulfuric acid		$H_2SO_4 : SO_2$ Weight ratio
	ppm	$\mu g/m^3$	ppm	$\mu g/m^3$	
El Segundo:					
26 Jan	0.065	185	0.0016	6.4	0.035
6 Feb	0.061	174	0.0031	12.4	0.071
22 Jan	0.062	177	0.0050	20.0	0.112
8 Feb	0.062	177	0.0054	21.6	0.112
10 Feb	0.055	158	0.0050	20.0	0.127
31 Jan	0.120	342	0.0046	18.4	0.054
11 Feb	0.102	291	0.0047	18.8	0.064
28 Jan	0.110	313	0.0055	22.0	0.070
15 Feb	0.125	356	0.0068	27.2	0.076
9 Feb	0.130	371	0.0075	30.0	0.081
30 Jan	0.205	584	0.0048	19.2	0.032
2 Feb	0.194	553	0.0098	39.2	0.071
Los Angeles:					
24 Mar	0.057	162	0.0048	19.2	0.118
21 Mar	0.067	191	0.0070	28.0	0.146
22 Mar	0.063	180	0.0072	28.8	0.160
10 Mar	0.057	162	0.0080	32.0	0.200
9 Mar	0.064	182	0.0092	36.8	0.201
13 Mar	0.065	185	0.0099	39.6	0.214
14 Mar	0.050	143	0.0084	35.2	0.246
22 Mar	0.122	348	0.0072	28.8	0.082
13 Mar	0.122	348	0.0126	50.4	0.145

dioxide increases. In El Segundo, a maximum sulfuric acid concentration of about 25 $\mu g/m^3$ was observed when the sulfur dioxide concentration was between 425 and 570 $\mu g/m^3$ (0.15 and 0.20 ppm), whereas, in downtown Los Angeles, a maximum sulfuric acid concentration of about 30 $\mu g/m^3$ was observed when the sulfur dioxide concentration was between 140 and 280 $\mu g/m^3$ (0.05 and 0.10 ppm).

During the past nine years the National Air Surveillance Networks have taken simultaneous measurements of 24-hour average sulfur dioxide and suspended sulfate in various cities.[34-36] Unpublished analyses of these data show that correlation coefficients between sulfur dioxide and suspended sulfate (sulfuric acid and sulfate salts) range between 0.5 and 0.9. Manganese and iron in the suspended particulate matter, relative humidity, and temperature were studied as variables that might affect this correlation. As relative humidity and the concentration of metals increased, so did suspended sulfate. Temperature had no effect on suspended sulfate concentrations.

The data from field studies thus agree essentially with data from laboratory investigations; both show that sulfur dioxide can be oxidized to sulfuric acid or a salt of the acid in the atmosphere. The field studies show, from evidence taken in a number of geographical locations, that a relationship exists between sulfur dioxide and sulfuric acid concentrations in the air. The relationship is dependent partly upon the amount of moisture in the air, partly upon the time the sulfur contaminants have been in the atmosphere, the amount of catalytic particulate matter present in the air, the amount (intensity and duration) of sunlight, the amounts of hydrocarbons and oxides of nitrogen, and the amount of directly reactive and adsorptive materials in the air, as well as on the extent of recent precipitation.

D. ACIDITY OF RAINWATER AND PARTICULATE MATTER

Gorham[37] studied the acidity (pH) of rainfall in two cities of England and found that it was more strongly related to the chloride content than to the sulfate content. Such a study apparently has not been made in the United States; however, examination of some rainfall samples collected by the National Air Surveillance Network showed pH values around 3. The National Air Surveillance Network data indicate that the chloride content of suspended particulate matter is generally very low in atmospheres of the United States[38] except along coastal areas.

In another set of unpublished data collected by the National Air Pollution Control Administration, sulfate accounted for 21 percent of the variation in pH of solutions of the suspended particulate matter, with an increase of 12 $\mu g/m^3$ of sulfate reducing the pH by 1 unit. The pH values in both sets of data ranged from approximately 4 to 7.5. In the presence of substantial amounts of ammonia, calcium carbonate, hydroxide, or other alkaline material, most of the sulfate is in salt form. The similarity of the magnitude of atmospheric sulfuric acid concentrations, when compared with the magnitude of total sulfate concentrations, indicates that in some atmospheres a large part of the total sulfate may be sulfuric acid.[32-35,39]

In Scandinavia, the acidity of rainfall and groundwaters has reached the point of causing great concern among many knowledgeable persons. Between the years 1955-1965, the average pH of rainfall decreased 1 unit--from 5.5 to 4.5. An alarming reading of pH 2.85 was made near Uddevalla in June 1967. The average value in western Sweden for the period June-August 1967 was pH 3.2.[40]

The implications of continued increase in acidity of rainfall and groundwaters for aquatic life, forests, stability of soils, etc. are serious indeed. The cause is directly related to the sulfur content of fuels used in Great Britain and continental power sources.[40]

Measurements of acidity of dustfall, though seldom reported, indicate that dustfall may be capable of providing a few kilograms of hydrogen ions and a few hundred kilograms of sulfate ions per hectare per year.[41-43] The importance of this to soil management is difficult to evaluate because of the heterogeneity of soils, their generally great buffering capacity, and the probably large, though unknown, buffering capacity of the dustfall itself. An order of magnitude estimation of the effect of acidity in dustfall is that approximately twice as much lime might have to be applied to the soil in areas near large cities, as to the soil of rural areas. This assumes that the near-urban areas have average annual sulfate deposits of eight to twelve tons per square kilometer per month (300 to 450 kilograms per hectare per year). An approximately tenfold reduction in sulfate deposit would be requied to reduce it to about the amount removed by plants and leaching.[44,45] Even though sulfur in some compounds is a major plant nutrient and is used as a fertilizer element under certain conditions, it would seem that uncontrolled deposition of sulfate from air pollution is undesirable.[46]

E. SUMMARY

Two major programs for the surveillance of atmospheric sulfur dioxide on a nationwide basis are operated by the U.S. Public Health Service and are (1) the National Air Surveillance Networks (NASN), in which 24-hour samples are obtained from about 100 sites 26 times a year, and (2) the Continuous Air Monitoring Project (CAMP), in which 5-minute average concentrations are recorded continuously in six large U.S. cities--Washington, Philadelphia, Cincinnati, Chicago, St. Louis, and Denver. The NASN program employs the colorimetric (i.e., West-Gaeke) method of analysis, while the CAMP program uses the electroconductivity technique and recently has added continuous, colorimetric (West-Gaeke) SO_2 monitoring devices at all six locations.

Levels recorded in CAMP cities over the period from 1962 to 1967 show mean annual concentrations ranging from 0.027 mg/m^3 (0.01 ppm) in San Francisco, to 0.49 mg/m^3 (0.18 ppm) in Chicago, with the averages exceeding, for 1 percent of the time, a concentration range between 0.24 mg/m^3 (0.09 ppm) and 1.8 mg/m^3 (0.68 ppm) for the different cities. The NASN annual average concentrations ranged from 5.4 μg/m^3 (0.002 ppm) in Kansas City, Missouri, to 0.46 mg/m^3 (0.17 ppm) in New York City. The highest 24-hour average concentration was 1.0 mg/m^3 (0.38 ppm), also in New York City, while the lowest 24-hour averages were below the minimum value detectable by the instruments--below approximately 3 μg/m^3 (0.001 ppm). Geographically, the highest values were recorded in the northeastern part of the United States, especially east of the Mississippi River and north of the Ohio River, where large quantities of high-sulfur fossil fuels are burned.

Extensive monitoring programs, such as those described above, yield large quantities of data. Information expressed in terms of average or maximum values does not give as complete a picture of air quality as does frequency distribution information, which shows the percentage of time that concentrations exceed specified levels. For a given averaging time, measurements of sulfur dioxide concentrations follow a log-normal frequency distribution. The two statistical parameters used to describe this distribution are the geometric mean and the standard geometric deviation. CAMP data covering eight cities from 1962 to 1967 show that, as averaging times become shorter, higher maxima and lower minima are obtained. This happens because, for shorter intervals, instantaneous fluctuations have greater effect on the recorded values. The standard geometric deviation, which is an index of the deviation of the samples from their geometric mean, therefore is greater for shorter averaging periods.

Based on data from eight CAMP cities, the 1-hour maximum value for the year is expected to be about 10 to 20 times the annual average, corresponding to standard geometric deviations of 2 and 2.5, respectively. Similarly, the 8-hour maximum ranges from about 6 to 10 times the annual mean; the one-day maximum ranges from 4 to 7 times the annual mean; and the maximum monthly average ranges from about 1.5 to 2 times the annual mean.

The CAMP data appear to be fairly representative of large U.S. metropolitan areas, but, for a city with a deviation outside these boundaries, a method exists to calculate the expected maximum concentrations, providing the averaging times are 1 hour or greater.[3] It is possible also to calculate the minimum concentration for a given averaging time, as well as the concentrations at various percentiles. These calculations make use of the geometric mean and the standard geometric deviation of samples obtained at a particular averaging time. It appears that a fairly good approximation of the frequency distribution of hourly averages over a year may be obtained with samples covering 24-hour periods on 22 randomly selected days.

Frequency data on the percent of the time that certain concentrations are exceeded usually necessitate the use of a computer but provide a very detailed description of air quality . For a given percentile, the concentrations measured over different averaging times usually vary. However, for the 30-percentile point, i.e., the value which is not exceeded for 70 percent of the time, the concentration appears to be about the same for all averaging times. Thus the 30-percentile value might be used as an indicator of the "general sulfur dioxide level" of a city, an index useful for ranking one city against another.

The ratio of the maximum sulfur dioxide concentration to the average value may be greater for measurements made near a single point source than for a city as a whole. For averaging periods from 4 to 54 minutes, for example, the maximum concentrations encountered near a point source were, respectively, 30 to 160 times the 6-month average value. These ratios are considerably higher than those calculated from the data for eight cities and 6 years shown in Table 2-2, and they demonstrate the kind of impact that a point source may have.

Hourly average concentrations of sulfur dioxide as high as 7.8 mg/m^3 (2.9 ppm) have been measured 0.8 kilometer from a coal-fired power plant. In general, concentrations decrease as (1) the distance from a source increases, and (2) the averaging time is extended. When averaged over many hours or days, concentrations measured several kilometers from a large source may be only a few micrograms per cubic meter. Near the point of discharge, power plants, oil refineries, smelters, and sulfuric acid production units may yield high ground-level sulfur dioxide concentrations.

Sulfur dioxide is partially oxidized to sulfuric acid in the atmosphere. The ratio between the two substances is dependent, among other things, on the oxidation rate, which in turn is dependent on the sunlight available and the concentration of moisture, catalysts, hydrocarbons, nitrogen oxides, and the quantity of directly reactive and adsorptive materials in the air. Recent precipitation also has an effect, as does the time various sulfur contaminants have been in the atmosphere.

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Chapter 3

EFFECTS OF ATMOSPHERIC SULFUR OXIDES ON MATERIALS

A. INTRODUCTION

Atmospheres polluted with sulfur dioxide have been found to be among the most corrosive of all atmospheres studied, and to be even more corrosive than some marine atmospheres.[1,2]

In reviews of the effects of air pollution on materials, Yocom and McCaldin,[3] and Burdick and Barkley[4] discuss the damage to metals, building materials, leather, paper, and textiles by the oxides of sulfur. Much of this damage is due to the conversion of sulfur oxides to highly reactive sulfuric acid. The combined action of sulfur oxides and particulate matter is discussed in the companion report Air Quality Criteria for Particulate Matter.

B. EFFECTS ON PAINTED SURFACES

Holbrow[5] found that the drying times of linseed, tung, and bodied dehydrated castor oil paint films exposed to 2.7 to 5.2 mg/m^3 (1 to 2 ppm) SO_2 were increased by 50-100 percent. At higher concentrations, 19 to 27 mg/m^3 (7 to 10 ppm), drying was delayed by up to two to three days. Oleoresinous and alkyd paints pigmented with titanium dioxide had both their touch-and hard-dry times increased substantially.

Based on these results Holbrow concluded that concentrations of SO_2 encountered in fogs or near industrial sites can increase the drying time and hardening time of certain kinds of paint systems. Some films become softer and others more brittle than those dried in the absence of SO_2--a factor likely to influence subsequent durability.

C. DAMAGE TO METALS

Under normal conditions damage to metals by the oxides of sulfur increased with increasing relative humidity and temperature.[6] Particulate matter in the air also contributes to the deleterious effects. Sulfur oxides generally accelerate corrosion by first being converted to sulfuric acid, either in the atmosphere itself or on metal surfaces. The corrosion products are mainly sulfate salts of the exposed metals.[7-10] In addition, atmospheric sulfuric acid can react with some suspended particles to form sulfate salts that also can accelerate corrosion of many metals.

Laboratory studies were carried out by Preston and Sanyal[11] using polished steel test panels. After being cleaned, degreased, and polished, the panels were contaminated with finely divided particles of various compounds. These consisted of various powdered oxides, chlorides, sulfates, and chromates, as well as boiler and flue dust particles commonly found in the atmosphere. Some panels were coated with varnish and other organic materials after the contamination step. The panels were then exposed to clean air at various humidities and some to low (unspecified) concentrations of SO_2. Filiform corrosion, characterized by a filamental configuration, the primary phase in electrolytic corrosion, was noted in all cases. The extent of corrosion was dependent on relative humidity, being greatest between 70 and 90 percent R.H. in most cases. The addition of traces of SO_2 to the test atmosphere greatly increased the rate of corrosion in all instances.

Schikorr[12] observed that steel panels exposed in Berlin during the winter months initially corroded five times faster than similar panels first exposed during the summer months. The particulate levels were much higher in winter and this resulted in the production of a greater abundance of corrosion nuclei. Nevertheless, Schikorr attributed this greater rate of corrosion primarily to the greater concentrations of gaseous combustion products, including sulfur oxides, in the air and to the longer periods of specimen wetting during the winter.

Foran et al.[13] and Gibbons[14,15] found that, among several metals exposed to atmospheres ranging from rural to heavy industrial, carbon steels corroded most, followed in descending order by zinc, copper, aluminum, and stainless steel. Furthermore, they observed rather direct relationships between corrosion and oxides of sulfur pollution in several ambient atmospheres in which 2-year average lead peroxide candle sulfation rates ranged approximately from essentially 0 to 12 mg SO_3/100 cm^2-day. The increase in corrosion per unit increase in sulfation rates, e.g., of the maximum corrosion noted at 12 mg SO_3/100 cm^2-day, approximately one-half had occurred with steel and about one-fifth with zinc at 2 mg SO_3/100 cm^2-day. In terms of the measurements made by these investigators, a lead peroxide sulfation rate of 2 mg SO_3/100 cm^2-day is roughly equivalent to 0.2 mg/m^3 (0.08 ppm) of sulfur dioxide.

Hanie and Upham[16] showed that sulfur dioxide concentration is the major factor in controlling the rate of corrosion of zinc. A simple linear function of average relative humidity and average SO_2 concentration accounted for 92 percent of the variability in average zinc corrosion rates. This function suggested that zinc surfaces will not be wet, and thus no corrosion will occur, below an average relative humidity of 48.8 percent.

Upham[17] reported on studies in St. Louis and Chicago where mild low-carbon steel panels were exposed to the atmosphere at a number of sites. It was assumed that meteorological conditions within each metropolitan area are sufficiently uniform that the air pollution level is the major site variable influencing observed corrosion rates. Concomitant measurements of the pollution levels at each site were made. In both cities, high correlations were found between corrosion rates, as measured by weight loss, and sulfur dioxide concentrations measured by the West-Gaeke method. Sulfation rates in St. Louis, measured by lead peroxide candles, also correlated well with weight loss due to corrosion. In St. Louis, except for one exceptionally polluted site, corrosion losses averaged 30 to 80 percent more than in nonurban locations.

Figure 3-1 shows the weight loss in 100-gram panels exposed in Chicago at seven sites for 3-, 6-, and 12-month periods and the corresponding mean concentration of sulfur dioxide measured at each site. Over the 12-month exposure period, the corrosion rate at the most corrosive site (mean SO_2 level of 0.32 mg/m^3 (0.12 ppm) was about 50 percent more than at the least corrosive site (mean SO_2 level of 0.08 mg/m^3 (0.03 ppm)). A regression analysis on the Chicago data relating corrosion, as measured by weight loss, to mean SO_3 concentrations resulted in the following regression equation:

$$y = 54.1s + 9.5 \qquad (3\text{-}1)$$

where

y is corrosion weight loss in grams per hundred gram panel (4 in. x 6 in. x 0.035 in. dimensions) and

s is mean SO_2 concentration in mg/m^3.

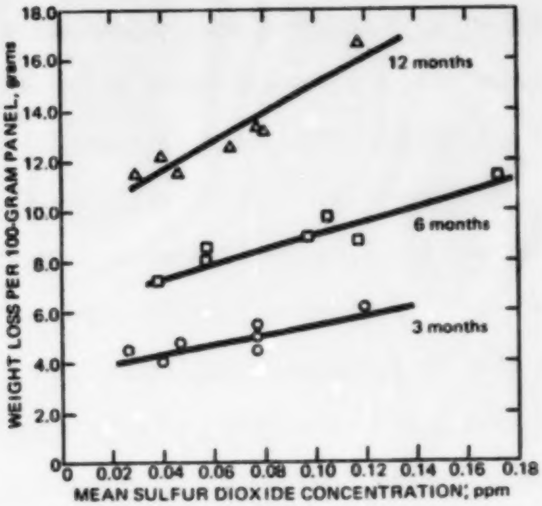

Figure 3-1. Relationship between corrosion of mild steel and corresponding mean sulfur dioxide concentration for 3-, 6-, and 12-month exposures at seven Chicago sites (Sept. 1963-1964).

The regression coefficient was statistically significant at the one-percent level. The linear relationship expressed by this equation would be valid only over the range of the observed data (i.e., from (0.08 to 0.32 mg/m^3 (0.03 to 0.12 ppm) mean annual concentration) and in locations with topography and climate similar to those of Chicago. The relationships were linear also in St. Louis, although the slope for the 3-month exposure period was greater than that in Chicago, presumably because the 3-month exposure took place during the winter months in St. Louis and during the autumn in Chicago. Differences between the two cities in terms of climate and exposure site configuration also may have influenced the results.

Suspended particulate levels were measured in Chicago at all seven sites with high-volume samplers, and these values correlated with corrosion rates. Since sulfur dioxide concentrations and particulate concentrations themselves tend to correlate, a covariance analysis was carried out to determine the relative influence of these two pollutants. This adjusted analysis indicated that the difference in corrosion rates at the various sites resulted primarily from differences in sulfur dioxide concentrations and not from differences in particulate levels. Thus, sulfur dioxide levels appeared to have the dominant influence on corrosion rates. Dustfall measurements made in St. Louis did not show a statistically significant correlation with corrosion rates.

The economic significance of metal corrosion has not been adequately investigated. In England, it has been estimated that about one-third of the annual replacement cost for steel rails is air pollution.[18] Couy[19-21] investigated the effect of atmospheric corrosion on maintenance and economics of overhead line hardware and guy wires in Pittsburgh. The conditions of actual materials in use over the period roughly from 1920 to 1940 were determined for areas of severe and average pollution. Areas of severe pollution included valleys traversed by railways and areas in direct wideline with industrial fumes. Formulae were developed to determine the amount of inspection required, the materials needed, and the costs involved for a particular situation. No direct cost estimates were made but it appeared that the life of the materials in the severely polluted areas was reduced to about two-thirds of that of the materials in the areas of average pollution. The average annual sulfur dioxide concentration during the period of the study was initially high ((0.4 mg/m^3 (0.15 ppm)) but had declined to approximately 0.14 mg/m^3 (0.05 ppm) by 1940 (0.11 mg/m^3 (0.15 ppm) in 1963).[22]

The effects of air pollution on electric contacts result in increased costs because of the losses associated with increased resistance of contacts having corrosion films and because more costly, less reactive, metals must be used. The use of gold instead of silver for contacts costs about 14.8 million dollars annually. If gold could be replaced by palladium, an annual savings of $8 million would result, but palladium tarnishes in a sulfur dioxide atmosphere.[23]

D. EFFECTS ON BUILDING MATERIALS

No recent work has been done on the effects of ambient concentrations of sulfur oxides on building materials. Early work,[4,24-26] however, shows that sulfur oxides may be associated with damage to various building materials. Sulfur dioxide, in the presence of moisture, is converted to sulfurous or sulfuric acids, which are capable of attacking a wide variety of building materials, including limestone, marble, roofing slate, and mortar.[27-29] Sulfuric acid attacks carbonate-containing stone by converting the carbonates into relatively soluble sulfates which rainwater then leaches away. Other types of stone, such as granite and certain sandstones, in which the grains are cemented together with materials containing no carbonate, are relatively unaffected by sulfur oxides in the atmosphere.[29]

Building stones erode to a greater or lesser degree according to their chemical composition. Softer building stones, such as the limestones and dolomites, are attacked more readily by the acids formed by the interaction of industrial smokes (even in small quantities) and moisture.[30] The dolomites contain both calcium and magnesium carbonates, the latter being readily soluble in an acid environment; the dolomitic stones are thus more vulnerable.[25,30,31] The calcium sulfate formed on the surface of masonry is about twice as bulky as the carbonate of the stone from which it was formed, so the stone appears to grow leprous.[30] Granites, gneiss, and many sandstones, which do not contain carbonates, and well-baked bricks, glazed bricks, and glazed tiles are attacked less readily by the sulfurous and sulfuric acids from the atmosphere. Additionally, serious disintegration of stone, caused in part by the expansion due to corrosion of iron tie rods, can occur.[25] Slates containing carbonates and the calcareous sandstones often used as roofing materials are also attacked by polluted acid atmospheres.[25] Decay occurs mainly on the undersides, especially between the laps, where moisture is held as a thin film.

Baines[24] reported that the expansive force, which developed from the crystallization of calcium and magnesium salts along the cleavage planes of stones in the buildings in various English cities, slowly opened up the old sealed vents where they could be attacked by atmospheric acid, and even lifted fragments of stone several tons in weight. On the British Houses of Parliament, which were approximately 90 years old when the survey was made, he found sulfate, which could only have been derived from the attack upon the stone by atmospheric acid, in cracks and fissures as much as 50 centimeters from the surface. He observed that the increase in the volume of crystallization of from 1 to 4.2 had thrown off great pieces of stone. Over 35 tons of stone were picked off portions of the building without using tools.

The deterioration of some of the finest monuments of antiquity and thousands of pieces of sculpture and carving in the open, on public buildings, and on cathedrals is a matter of increasing concern. The rate of decay has accelerated in recent years because of the increased pace of Twentieth Century industrialization and larger emissions of combustion products containing sulfur oxides and particulate matter. Cleopatra's Needle, the large stone obelisk moved from Alexandria, Egypt, to London, has suffered more deterioration in the damp, smoky acid atmosphere of London in 70 to 80 years than in the earlier 3,000 or more years of its history.

E. EFFECTS ON TEXTILE FIBERS, DYES, AND MISCELLANEOUS MATERIALS

The vulnerability of textile fabrics and furnishings to acid products of combustion, which are often sorbed on the particles emitted simultaneously by combustion sources, depends on the chemical composition of the textiles.[31] Cellulosic vegetable fibers, such as cotton, linen, hemp, jute, rayons, and synthetic nylons, are particularly sensitive to acid products of combustion such as sulfurous and sulfuric acids. After exposure to these acids, such fibers lose tensile strength.[32] Animal fibers, such as wool and furs, are more resistant to acid damage.[32]

Brysson et al.[33,34] in both laboratory and out-of-door experiments over a 12-month period, demonstrated a direct correlation between air pollution and the accelerated degradation of exposed cotton fabrics. In heavily contaminated sites the degradation rate was four to five times that of the least polluted sites. Sulfation and sulfur dioxide concentration in the atmosphere showed the best degree of correlation with fabric degradation and soiling. The other air pollution measurements--dustfall and suspended particulate matter--also correlated but to a lesser degree.

Zeronian et al.[35] similarly exposed synthetic fibers to contaminated atmospheres. The greatest degradation occurred in the exposure of nylon to sulfur dioxide. The breaking load, rupture energy, and breaking extension of yarn samples removed from the nylon fabric were markedly reduced. The evidence revealed that SO_2 apparently can degrade nylon without the presence of particulate matter. Furthermore, it was found that the degradation of the samples was not due to hydrolysis following conversion of the SO_2 to sulfuric acid. They found further that modacrylic was not affected by any of the gases studied (SO_2, O_3, NO_2) and that polyester was not affected by either SO_2 or O_3.

Dyed fabrics containing certain classes of dyes are attacked by acid compounds often sorbed on atmospheric particles; the dye coloring is reduced or sometimes destroyed entirely. Color changes of dyed fabrics exposed without sunlight to the atmospheres of Los Angeles, Chicago, Phoenix, and Sarasota, Florida, were studied during the period October through December, 1961.[36,37] For some dyes, maximum and severe fading occurred in Chicago, where sulfur dioxide concentrations were highest (NASN annual average about 0.25 mg/m^3 (0.09 ppm)).[38,39]

In controlled environment studies,[40] selected dye-fabric combinations were exposed to a variety of pollutants (in the absence of light) in order to assess dye fading characteristics. Auto exhaust showed no fading; clean air plus SO_2 (2.7 mg/m^3 (1 ppm)) showed no fading; irradiated auto exhaust produced significant fading in some dyes; and irradiated auto exhaust plus SO_2 (2.7 mg/m^3 (1 ppm)) gave rise to fading in additional dyes as well as more pronounced fading in those dyes that faded without SO_2. This shows the positive synergistic effect of SO_2, and again emphasizes that in many cases damage is a function of pollutants working together rather than by themselves.

Leather has a strong affinity for SO_2, which causes it to lose much of its strength and ultimately to disintegrate. The storage of valuable leather-bound books in city libraries can pose a serious problem. Book bindings stored in rooms with a free exchange of polluted air were found to deteriorate much more rapidly than those stored in confined spaces or inside of glass cases.[25]

Paper also absorbs SO_2 which is oxidized to sulfuric acid. The sulfuric acid causes discoloration and renders the paper brittle and fragile.[25] Exposures to SO_2 (5.5 to 24 mg/m^3 (2 to 9 ppm)) for 10 days resulted in embrittlement and a decrease in folding resistance of both book and writing paper.[4]

F. SUMMARY

Although more quantitative data presenting dose-response relationships are needed, sufficient evidence exists to conclude that atmospheres polluted with oxides of sulfur directly and indirectly attack and damage a wide range of materials and property. Much of this damage is due to the conversion of sulfur oxides to highly reactive sulfuric acid.

In the laboratory, steel test panels dusted with particles commonly found in polluted atmospheres (e.g., powdered oxides, boiler and flue dusts, and chloride, sulfate, and chromate salts) corroded at a low rate in clean air at relative humidities below 70 percent. The corrosion rate increased at humidities higher than 70 percent, and it greatly increased when traces of sulfur dioxide were added to the laboratory air.

Corrosion rates of most metals--especially iron, steel, and zinc--are accelerated by sulfur dioxide-polluted environments. Particulate matter, high humidity, and temperature also play an important synergistic part in this corrosion reaction. Atmospheric corrosion studies show increased corrosion rates in industrial areas where air pollution levels, including sulfur dioxide and related pollutants, are higher. Further, corrosion rates are higher in the fall and winter seasons when particulate and sulfur oxides pollution is more severe due to a greater consumption of fuel for heating. Depending on the kind of metal exposed as well as location and duration of exposure, corrosion rates were 1-1/2 to 5 times greater in polluted atmospheres than in rural environments.

In Chicago and St. Louis, where steel panels were exposed at a number of sites, high correlations were found in each city between corrosion rates, as measured by weight loss, and sulfur dioxide concentrations. In St. Louis, except for one exceptionally polluted site, corrosion losses averaged 30 to 80 percent more than in nonurban locations. Over a 12-month exposure period in Chicago, the corrosion rate at the most corrosive site (mean SO_2 level of 0.32 mg/m^3 (0.12 ppm)) was about 50 percent more than at the least corrosive site (mean SO_2 level of 0.08 mg/m^3 (0.03 ppm)). Sulfation rates in St. Louis, measured by lead peroxide candle, also correlated well with weight loss due to corrosion. Although suspended particulate levels measured in Chicago with high-volume samplers correlated with corrosion rates, a covariance analysis indicated that sulfur dioxide concentrations were the dominant influence on corrosion. Measurements of dustfall in St. Louis did not correlate significantly with corrosion rates. Based on these data, it appears that considerable corrosion may take place (i.e., from 11 to 17 percent weight loss in steel panels) at annual sulfur dioxide concentrations in the range of 0.08 to 0.32 mg/m^3 (0.03 to 0.12 ppm) and, although high particulate levels tend to accompany high sulfur dioxide levels, the sulfur dioxide concentration has a greater influence on the degree of corrosion that takes place.

Qualitative examples of effects resulting from corrosion by sulfur dioxide include:

1. A one-third reduction in the life of overhead power line hardware and guy wires;
2. The necessary use of more expensive, less corrodible metals such as gold in some electrical contacts; and
3. One-third of the annual damage to steel rails in England.

Atmospheres containing oxides of sulfur also attack and damage a wide variety of building materials--limestone, marble, roofing slate, and mortar--as well as statuary and other works of art, causing discoloration and actual physical deterioration. Certain textile fibers--such as cotton, rayon, and nylon--are also harmed by atmospheric sulfur oxides, and in the presence of other pollutants, fading of dyed fabrics may occur. Severe fading was noted for some dyes in fabrics exposed in Chicago, where annual average sulfur dioxide levels were 0.24 mg/m^3 (0.09 ppm). Leather exposed to sulfur dioxide may lose much of its strength while paper becomes discolored and brittle.

Concentrations of 2.7 mg/m^3 (1 ppm) SO_2 can increase the drying time of some oil-based paints by 50 to 100 percent. Some films become softer and others more brittle, a factor likely to influence subsequent durability.

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Chapter 4

EFFECTS OF ATMOSPHERIC SULFUR OXIDES ON VEGETATION

A. INTRODUCTION

Extensive experiments and observations have been made for over one hundred years on the effects of sulfur dioxide on vegetation by investigators in all parts of the world. Substantial reviews of vegetation injury from the oxides of sulfur have been made by Thomas,[1-4] Sheffer and Hedgcock,[5] Brandt and Heck,[6] Katz and McCallum,[7] and Daines.[8] Summaries of acute effects on a large number of plant species susceptible to sulfur dioxide injury are given by Wood[9] and in the Environmental Biology Volume of Biological Handbooks.[10] Although Thomas[4] stated that the effects of sulfur dioxide on plants are fairly well understood, there are still some points of unresolved controversy in the literature. The response of plants to sulfur dioxide presents a many faceted problem[8] and involves the interactions of plant characteristics, environmental conditions, and dosage of the toxicant.

According to Katz,[11] one of the first descriptions of sulfur dioxide injury to plants was by Schroeder and Reuss in 1883. Descriptions of injury have appeared in numerous publications since that time.[6-8,12-14] Two general types of injury are produced by sulfur dioxide, acute and chronic.[1,6-8] Any overall effect on growth and production is apparently associated with some degree of acute injury from sulfite or sulfurous acid or to chronic injury resulting from accumulation of sulfates.[14]

B. SYMPTOMS IN VEGETATION OF EXPOSURE TO SULFUR DIOXIDE

1. Acute Injury

Acute injury results from the rapid absorption of toxic concentrations of sulfur dioxide.[14] Immediately after exposure, tissues in sharply defined marginal and intercostal area take on a dull water-soaked appearance.[1] These areas subsequently dry out and bleach to an ivory color. On some species the lesions finally become brown to reddish-brown.[4,6,15,16] A sharp line usually separates the injured lesion from surrounding, apparently healthy, leaf tissue. Injury seldom extends across the veins of broad-leafed plants unless the injury is severe.[2]

Acute injury in pine usually occurs in bands on the tips of needles with the injured area taking on a reddish-brown color.[7] The injured area changes from the usual dark green color to a lighter green, then definite areas turn yellowish-brown and finally reddish-brown, giving the banded appearance. The discoloration in conifers may involve the whole needle or limited areas of any portion. Abscission may follow after some interval and the affected trees are often deficient in needles.

The basic bleached and collapsed blotches described on broad-leafed plants are, however, also typical on grass foliage.[17,18] The final bleached pattern between the parallel veins of grass leaves gives a streaked effect. Often only the principal vein or "midrib" remains intact. The collapsed lesion generally extends uniformly through the entire thickness of the leaf blade.

Holmes et al.[12] found that barley, growing in the field, was severely injured by fumigations with 14 mg/m^3 (5 ppm) sulfur dioxide administered one hour a day on six successive days. If the same total dosage was applied for much shorter intervals during the six days, there was much less injury. Apparently injury could be repaired if sufficient periods free of toxicant were provided. Zahn[19] confirmed this decrease in damage with shortened exposure times and that a longer recovery period between exposures also reduces the plant damage. It was also reported that injury to very young barley plants did not reduce final yield but that injury late in the life of the plants caused significant reduction in yield. No yield reduction occurred unless visible damage symptoms were detected on the foliage.

2. Chronic Injury

Sublethal concentrations of sulfur dioxide may require several days or weeks to cause the development of the gradual yellowing or chlorotic symptom of chronic injury.[2] The slow fading of green color over a period of several days suggests that the chlorophyll-making mechanism is being destroyed and that the green pigment cannot be replenished. If only a few cells in an area are affected, the area may become chlorotic or brownish-red. A large amount of sulfate is found in leaves with chronic symptoms,[14] whereas leaves which are acutely injured show only a small increase in sulfate content. Large quantities of sulfate may be accumulated in leaf tissue without causing injury.[14,20] Yet, if excessive amounts are absorbed rapidly, acute injury results.

Sulfur dioxide is very soluble in water and is absorbed by leaves. If absorbed slowly it is oxidized or perhaps reduced to a small extent.[14] The sulfuric acid resulting from oxidation and hydrolysis in the leaf tissue is rapidly metabolized by organic bases. Acids formed in the leaf tissue may reduce the buffer capacity without changing pH and when the buffering capacity is exceeded, chlorosis results. A recent report[21] indicates that the reduction of sulfur dioxide in the leaf tissue may have more significance than previously proposed by Thomas,[14] since considerable hydrogen sulfide was given off by tomato plants during, and for a time after, fumigation with sulfur dioxide.

3. Physiological Effects

The "invisible injury" theory suggesting that suppression of growth and yield may occur because of long-term low concentration exposure to sulfur dioxide, even if visible symptoms of foliage injury do not develop, was proposed by Stoklasa.[22] According to Setterstrom,[23] this theory was supported by several investigators, including Wieler, Bredemann, Janson, and Bleasdale. Many investigators accept the thesis that growth and yield are not affected unless visible symptoms of injury occur on the foliage.[1,2,6,24-26] There is a straight-line relationship between yield of alfalfa and either the total area destroyed by acute symptoms or the area covered by the chlorotic symptom.[27] The amount of yield reduction produced by sulfur dioxide symptoms can be duplicated by clipping a comparable amount of leaf area from healthy plants.[16] Destruction of portions of the leaf area and accompanying defoliation not only reduce yield of the current crop but may adversely affect the next one or two clippings.

Reduction in growth of pine trees in the vicinity of sulfur dioxide sources has been reported.[7,20,28] This growth reduction was evidently due to heavy defoliation and destruction of portions of needles during prolonged exposure to levels of sulfur dioxide sufficient to kill cells and tissue or to build sulfate concentrations to a level which destroyed chlorophyll. Needles of many conifers are normally retained for three or more years and accumulate sulfate from continued low concentrations of sulfur dioxide. Needle drop is stimulated by high levels of sulfates, and trees growing near sulfur dioxide sources often have very sparse foliage.[20]

Defoliation of citrus trees exposed to sulfur dioxide has been observed in Japan.[29] Defoliation increased with increasing concentrations, and increased sulfur content of foliage coincided with the rate of defoliation. It was concluded that leaf analyses for sulfur content may be useful for evaluating chronic injury, but such analyses could not be used for evaluating acute injury. A lower rate of absorption may produce symptoms of chlorosis and reduce CO_2 exchange, causing temporary disruption of photosynthesis and respiration. The rate of carbon dioxide exchange returns to normal soon after the toxicant is removed if visible symptoms do not develop. At very low concentrations, the sulfur oxides may be utilized by plants deficient in sulfur causing stimulation of growth and production.[14,23,26]

4. Mechanism of Injury

The mechanism by which sulfur dioxide causes injury to leaf tissue is not thoroughly understood, although a number of suggestions have been made. The acute symptoms are generally attributed to excessive sulfite or sulfurous acid in the tissue.[1,14] With a high rate of absorption, sulfite is thought to accumulate; sulfurous acid is then formed and subsequently attacks the cells. Fulfur dioxide enters the leaf through the stomata and is thought to be oxidized, perhaps by oxygen, a by-product of photosynthesis.[25] Sulfuric acid is then formed and reacts with organic bases.[14] The resulting sulfates are apparently translocated with the transpiration stream and deposited at the tip or edges of the leaf. Haselhoff and Lindau[30] suggested that sulfur dioxide attaches itself to aldehydes and sugars in the leaf and as these products degrade, sulfurous or sulfuric acid is formed and injury results. Dorries[31] reasoned that local acidity from the sulfur dioxide split magnesium from the chlorophyll molecule and formed pheophytin. Noack[32] suggested that iron in the chloroplasts was inactivated by sulfur dioxide, causing interference with the assimilation of organic compounds by the plant.

C. SUSCEPTIBILITY OF VEGETATION TO SULFUR DIOXIDE

Different species, different varieties within a plant species, and even individuals within a plant variety vary considerably in their susceptibility to sulfur dioxide.[6,8,14] Thomas[2-4] tabulates many plants according to their sensitivity to sulfur dioxide. Since alfalfa is one of the most sensitive plants, it was used as a reference species and all other species and varieties were compared with it. The order of sensitivity was calculated by Thomas and Hill[27] from unpublished data of O'Gara on resistance factors for over 300 plants. According to Thomas and Hill,[27] O'Gara's method of determining resistance consisted of fumigating the plants for one hour with a measured concentration of sulfur dioxide just sufficient to cause traces of injury. A corrected threshold concentration for injury was calculated for 100 percent relative humidity. This calculated value was then divided by 2.1 mg/m^3 (1.25 ppm), which was the concentration required for incipient marking on alfalfa in the 1-hour period. The ratings range from alfalfa, barley, endive, and cotton, the most sensitive, with ratings of 1, through celery, citrus, and cantaloupe, with ratings of about 7, to privet leaves, the most resistant with a rating of 15. However, the ranges of resistance thus gained may undergo changes under field conditions.[33] It has become apparent, for instance, that types of larches in places of higher concentrations incur greater damage than gooseberries (Ribes uva-crispa), while in locations with low concentrations, the resistance conditions are reversed. The criterion applied for the appraisal of effect is of essential significance in studies of this type.

O'Gara's unpublished data and his fundamental equation for the "Law of gas action on the plant cell"[34] have been used extensively by Thomas[1,3,4,12,25] to calculate relative sensitivity of various plants to sulfur dioxide fumigation and to determine the effect on yield. O'Gara's formula was:

$$t(C-Co)=K \tag{4-1}$$

where t is time (hrs) through which the gas acts to produce a certain effect,

C is the concentration (g/m^3) of the gas,

C_o is the threshold concentration (g/m^3) of the gas for injury to the plant, and

K is a constant.

According to Thomas and Hill[27] the amount of injury caused by a given quantity of sulfur dioxide varies with the rate of absorption; that is, a given amount of gas, absorbed in a short time period, will cause more leaf destruction than if the absorption were to occur over a longer period. General time-concentration-absorption equations for data obtained from fumigations of alfalfa are proposed. By applying these equations to data from numerous fumigations, it was possible to calculate the dosage required to produce any observed degree of injury under conditions of maximum sensitivity. For example, equations representing incipient marking, 50 percent leaf destruction and 100 percent leaf destruction, under conditions of maximum sensitivity were:

$tC=0.94+0.24t$ (traces of leaf destruction appear),

$tC=2.1+1.4t$ (50 percent leaf destruction occurs), and

$tC=3.2+2.6t$ (100 percent leaf destruction occurs).

Injury thus begins after four hours of exposure to 1.2 mg/m^3 (0.45 ppm), etc. Curves constructed from these calculations are plotted in Figure 4-1. Guderian et al.[35] did not believe that the O'Gara equation fitted their observations and suggested that an exponential equation of the form

$$t=ke^{-a}(C-C_o) \qquad (4\text{-}2)$$

where k, a, and C_o are parameters varying with species and degree of injury, best described their data.

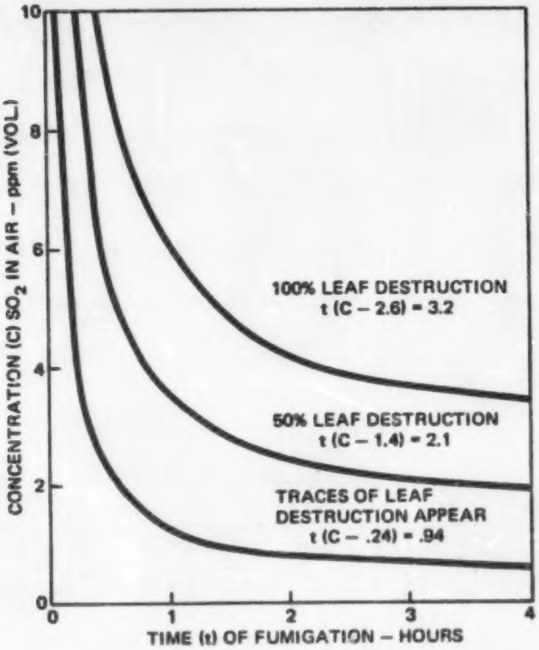

Figure 4-1. Curves showing concentrations of sulfur dioxide which will produce three different degrees of acute alfalfa leaf damage in different time periods under conditions of maximum absorption. (These curves from experimental data may be used to estimate the extent of damage to alfalfa at any sulfur dioxide concentration and exposure time.)

An apparatus was developed by Spierings[36] whereby susceptibility of trees and shrubs to air pollutants could be determined under natural conditions without disruption of prevailing climates. Fumigation experiments with sulfur dioxide showed that apple and pear varieties were the most susceptible of the fruit trees and that mountain ash was one of the most susceptible of the deciduous forest trees. Six-hour exposures of the fruit varieties to 1.3 mg/m^3 (0.48 ppm) produced injury, whereas injury to the mountain ash was produced by three-hour exposures to 1.5 mg/m^3 (0.54 ppm) of sulfur dioxide.

Sheffer and Hedgcock[5] reported injury to ponderosa pine, western larch, Pacific pinebark, and creambush rockspirea during an exposure to 1.4 mg/m^3 (0.5 ppm) for 7 hours. They concluded that the lowest concentration of sulfur dioxide that injures conifers is 0.68 mg/m^3 (0.25 ppm). Alfalfa is generally considered to be one of the most sensitive plants, and Thomas and Hill[16] reported that photosynthesis or respiration by alfalfa plants was not affected by concentrations up to 0.82 mg/m^3 (0.3 ppm) unless the exposure was so long that sulfate injury occurred. Katz and McCallum[7] reported that larch, one of the most sensitive conifers, developed slight symptoms from 0.82 mg/m^3 (0.3 ppm) sulfur dioxide in an 8-hour exposure. They concluded that if concentrations higher than 0.82 to 1.4 mg/m^3 (0.3 to 0.5 ppm) do not occur and if the duration of concentration at the 0.82 mg/m^3 (0.3 ppm) level is short in a single gas exposure, plant damage should not occur.

In the vicinity of the smelter at Trail, British Columbia, which in 1929 emitted an average of 18,600 tons of sulfur dioxide per month, plant injury was noted as far as 83 kilometers south of the smelter.[28] Three zones of injury were delineated on the basis of the percentage injury to ponderosa pine, Douglas fir, and forest shrubs: in Zone 1 there was 60 to 100 percent injury; in Zone 2, 30 to 60 percent injury; in Zone 3, 1 to 30 percent injury. Zone 1, in which injury was acute, extended about 48 kilometers south of the smelter in a river valley; Zone 3, at higher elevations, extended 83 kilometers south of the smelter and contained trees with relatively slight markings and trees suffering from slow but progressive deterioration. After sulfur dioxide control devices were installed, measurements in 1934 and again in 1935[28] showed that the injury to broadleaf trees and to shrubs had dropped to 20 percent in the former Zone 1 and to 4 percent in the former Zone 3. Appraisal of ponderosa pine cone production in 1936 revealed that 81 percent of the pines in Zone 1 had no cones and that outside the zone, 16 percent of the pines had no cones.[5] Sulfur dioxide concentrations 24 kilometers south of the smelter in Zone 1 averaged about 0.08 mg/m^3 (0.03 ppm) during the summer with occasional peak concentrations in excess of 1.4 mg/m^3 (0.5 ppm) for a total time of 5 to 10 hours.

Linzon[37] reported marked growth suppression and chlorotic needles on white pine at locations 40 kilometers and less from the Sudbury, Ontario, smelter where measurable sulfur dioxide concentrations were present from 10 to 20 percent of the time. Concentrations of sulfur dioxide above 0.68 mg/m^3 (0.25 ppm) were present less than 1 percent of the time; the remainder of the measurable concentrations were less than 0.68 mg/m^3. The annual average concentrations apparently ranged downward from 0.082 mg/m^3 (0.03 ppm).

Sullivan[38] reported damage to 36 percent of the home gardens in an area near a smelter in Australia where the annual average sulfur dioxide concentration was 0.024 mg/m^3 (0.009 ppm) and the maximum daily average 0.44 mg/m^3 (0.155 ppm). In another area more influenced by the smelter, 89 percent of the gardens were damaged; there the annual average was 0.090 mg/m^3 (0.033 ppm) and the maximum daily average 1.6 mg/m^3 (0.60 ppm). In the latter area, during brief fumigations, sulfur dioxide concentrations ranged up to 27 mg/m^3 (10 ppm).

Injury to at least 15 tree species, including both conifers and hardwoods, in the vicinity of petroleum refineries processing crude oil, which used 3-percent sulfur pitch residue in the refinery furnaces, was reported by Linzon.[39] Concentrations of sulfur dioxide measured in the atmosphere exceeded 1.4 mg/m^3 (0.5 ppm) during 10 hours in one month in this area with momentary peaks over 5.4 mg/m^3 (2 ppm). Slight to severe acute injury was reported for all species within 1.6 to 3.2 kilometers from the refineries.

Reports of deteriorated vegetation in areas polluted by sulfur dioxide[25,37,39] make it clear that injury can occur where annual average concentrations are very low when the sources of pollution and/or the meteorological conditions are such that threshold for injury is exceeded occasionally. The problem is economically serious with Scots pine forests in the Ruhr area.[40]

D. FACTORS AFFECTING PHYTOTOXICITY

The response of vegetation to sulfur dioxide as an air pollutant is influenced greatly by temperature, relative humidity, light intensity, soil moisture, nutrient supply, and age of plant or tissue exposed. Each of these factors is discussed below.

1. Temperature

A plant is much more resistant to sulfur dioxide at temperatures below 5° C.[23,26,41,42] Setterstrom and Zimmerman[41] found that buckwheat plants were equally susceptible to injury at 18° C and 41° C. Several investigators[11,23,29] have reported greater resistance in winter and have related this to lower physiological activity of the plants. Physiological activity of broad-leafed plants declines sharply as the leaves become senescent and drop in fall and winter, but activity is much higher in spring and early summer. Sensitivity to sulfur dioxide injury is similarly higher in spring.[11] Weaver and Morgensen[43] found that transpiration from conifers in winter was scarcely greater than from the defoliated stems of broad-leafed trees. Apparently the conifers are essentially dormant in winter and gas exchange by the needles is very low, thus increasing resistance to toxicants.

2. Relative Humidity

Although reports of various investigators do not show good agreement, susceptibility of plants to sulfur dioxide generally tends to increase with increases in relative humidity, providing light and soil moisture are not limiting.[11,23,25,41]

3. Soil Moisture

Minor variations in soil moisture during exposure have no detectable effect on susceptibility if there is sufficient moisture for normal plant growth.[41] When plants approach the wilting point, resistance increases significantly. Plants grown with an ample water supply are much more susceptible than plants grown with inadequate water.

4. Light Intensity

Plants in complete darkness are highly resistant to sulfur dioxide and the resistance decreases as the light intensity is increased up to 3,000 candles. Plants grown in shade before exposure to the toxicant are more susceptible than those grown in full sun.[13,23,25,41]

5. Nutrient Supply

Alfalfa plants grown in a deficient nutrient supply were more susceptible to sulfur dioxide than plants receiving adequate nutrients.[41]

6. Age of Plant Tissue

Young plants and newer foliage are much more resistant to sulfur dioxide than older leaves. Middle-aged leaves have highest susceptibility.[41]

E. SYNERGISTIC EFFECTS OF SULFUR DIOXIDE AND OZONE

Menser and Heggestad[44] demonstrated synergistic action between sulfur dioxide and ozone. Combinations of sublethal concentrations of sulfur dioxide (0.66 mg/m^3 (0.24 ppm)) and ozone (0.06 mg/m^3 (0.03 ppm)) in two-hour fumigations produced injury to tobacco plants. When the exposure time was doubled (4 hours), the severity of response was approximately doubled, but there was no response when fumigation consisted of either sulfur dioxide or ozone alone. Heck[45] found moderate to severe injury on tobacco from 4-hour exposures to 0.06 mg/m^3 of ozone in combination with 0.27 mg/m^3 (0.1 ppm) of sulfur dioxide. Middleton et al.[15] reported that the addition of small amounts of sulfur dioxide to polluted atmospheres in the Los Angeles Basin reduced the amount of injury produced in plants. He also reported that a ratio of sulfur dioxide to ozone less than

4:1 made the plants less susceptible to ozone damage; but if the ratio was 6:1 or higher, there was no evidence of interference with ozone susceptibility. Studies by Hindawi[46] substantiate the synergistic responses reported for ozone and sulfur dioxide. Heck[45] reported a synergistic reaction between nitrogen dioxide and sulfur dioxide. A 4-hour exposure to a mixture of 0.19 mg/m^3 (0.1 ppm) of nitrogen dioxide and 0.27 mg/m^3 of sulfur dioxide produced moderate injury to a sensitive tobacco variety. If there is a synergistic response between ozone and sulfur dioxide or other pollutants, it offers a partial explanation for occasional inconsistencies between findings in the laboratory with single agents and findings on plant response in the natural environment.

F. EFFECTS OF SULFURIC ACID MIST ON VEGETATION

Thomas et al.[2] discussed experiments in which plants were exposed to sulfuric acid mists in concentrations of from 108 to 2160 mg/m^3. Sulfuric acid droplets have settled on dry leaves without causing injury, but when the leaf surface was wet, a spotted injury has developed. Middleton et al.[15] and Thomas et al.[2] reported that this type of injury occurred in the Los Angeles area during periods of heavy air pollution accompanied by fog when the surface of the leaf may be wet. Injury may also occur in the absence of fog near combustion sources containing sulfur oxides when the effluent gas dew point permits acid droplet formation.

The sequence of symptom development is one in which the exposed surface, usually the upper surface, shows the initial necrosis. The pH of the leaf-surface moisture may be less than three. Cellular collapse in many small spots develops progressively through the upper epidermis, mesophyll, and lower epidermis of the leaf, leaving scorched areas. No glazing or bleaching accompanies this injury, and leaf areas covered by exposed leaves show no marking. In the Los Angeles area, swiss chard and beets have shown the most typical injury (described above) of all plant species examined. Alfalfa has also developed a spotted injury pattern. Spinach is more uniformly wetted by fog and has shown a more diffuse type of injury.

G. SUMMARY

Sulfur dioxide absorbed by plants may produce two types of visible leaf injury, acute and chronic. Acute injury, which is associated with high concentrations over relatively short intervals, usually results in the injured tissues drying to an ivory color, but sometimes they darken to a reddish-brown. Brownish discoloration occurs in the tips of pine needles, which may be followed by abscission, while broad-leaved plants and grasses show necrotic blotching. Chronic injury, which results from lower concentrations over a number of days or weeks, leads to a gradual yellowing (i.e., chlorosis, in which the chlorophyll-making mechanism is impeded) or pigmentation of leaf tissue. Generally, for growth and production to be affected, visible symptoms of injury, such as acute lesions, chronic chlorosis, or excessive leaf drop, also occur.

The mechanism by which acute injury occurs apparently involves the plant's ability to transform absorbed sulfur dioxide into sulfuric acid and then into sulfates which are deposited at the tip or edges of the leaf; with a high rate of absorption, sulfite is thought to accumulate, and sulfurous acid is then formed which subsequently attacks the cells. Chronic injury, on the other hand, results from the gradual accumulation of excessive amounts of sulfate in the leaf tissue. Sulfate formed in the leaf from sulfur dioxide absorbed from the atmosphere is additive to sulfate absorbed through the roots. Although levels of sulfate in some leaf tissue five to ten times above normal have been noted with no detectable symptoms of injury, very high levels cause chronic symptoms and stimulate leaf drop.

The amount of acute injury caused by sulfur dioxide depends on the absorption rate of the gas, which is a function of the concentration. Thus a given amount of gas absorbed in a short period (at a high concentration) will cause more leaf destruction than if the same amount of gas were absorbed over a longer period (at a lower concentration). Mathematical expressions have been worked out which, for some plant species, may be used to relate concentration, time of exposure, and amount of damage. Different varieties of plants vary widely in their susceptibility to sulfur dioxide injury. The threshold response of alfalfa to acute injury is 3.4 mg/m^3 (1.25 ppm) over one hour, whereas privet requires 15 times this concentration for the same amount of injury to develop. Some species of trees and shrubs have shown injury at exposures of 1.4 mg/m^3 (0.5 ppm) for seven hours, while injury has been produced in other species at 3-hour sulfur dioxide exposures of 1.5 mg/m^3 (0.54 ppm) and, in still others, at 8-hour exposures of 0.8 mg/m^3 (0.3 ppm). From such studies, it appears that acute symptoms will not occur if the maximum concentration for the year does not exceed 0.8 mg/m^3. From the data on the CAMP cities

(Chapter 2), an 8-hour maximum concentration of 0.8 mg/m^3 would correspond to a mean annual concentration of between 0.08 and 0.14 mg/m^3 (0.03 and 0.05 ppm).

Chronic symptoms and excessive leaf drop may be produced by long-term exposures to lower concentrations and have been reported in locations where the mean annual concentration is below about 0.08 mg/m^3 (0.03 ppm). Because chronic injury results from the slow buildup of sulfate in the tissue, leaf sulfate analyses may be a useful index for evaluating chronic injury.

The suppression of growth and yield usually is accompanied by visible symptoms of injury. A straight-line relationship, for example, has been found between the yield of alfalfa and the total area destroyed by acute symptoms or the area covered by the chlorotic symptoms. However, it has been suggested that, in some cases, sulfur dioxide might suppress growth and yield without causing visible injury. One investigator reported that yields of rye grass grown in unfiltered air were significantly lower than similar plants grown in filtered air, with no visible symptoms in the plants. Sulfur dioxide levels in the unfiltered air ranged from 0.03 to 0.11 mg^3 (0.01 to 0.06 ppm) with exposure periods ranging from 46 to 81 days, although it is not known whether other gaseous pollutants were present.

Sensitivity of plant materials is affected significantly by such environmental conditions as temperature, relative humidity, soil moisture, light intensity, nutrient level, and by sulfate content of the soil and irrigation water. At locations in the vicinity of point sources of sulfur dioxide, high concentrations occur with greater frequency and damage to plants is more likely to occur. Plant damage has been noted as much as 83 kilometers downwind from a smelting operation which emitted large quantities of sulfur dioxide. Slight-to-severe injury was reported to at least 15 tree species, including both conifers and hardwoods, in the vicinity of petroleum refineries where concentrations exceeded 1.4 mg/m^3 (0.5 ppm) during 10 hours in one month with momentary peaks as high as 5.4 mg/m^3 (2 ppm).

Sulfur dioxide concentrations from 0.27 to 0.68 mg/m^3 (0.1 to 0.25 ppm) will react synergistically with either ozone or nitrogen dioxide in short-term exposures (e.g., 4 hours) to produce moderate-to-severe injury on certain sensitive plants.

Sulfuric acid mist, which may occur in polluted fogs and mists, also damages leaves. The acid droplets cause a spotted injury to leaves which are wet due to fog conditions. Such injury may occur at concentrations of 0.1 mg/m^3.

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Chapter 5

TOXICOLOGICAL EFFECTS OF SULFUR OXIDES ON ANIMALS

A. INTRODUCTION

The toxicology of oxides of sulfur is reviewed in Chapters 5 to 7 of this document. Unfortunately, published data generally refer to concentrations far in excess of those likely to be found in polluted atmospheres, and therefore have little relevance to criteria for atmospheric pollutants. Even where the animal studies are carried out at more realistic levels, it is certain that the health hazard associated with community air pollution can only be evaluated directly in epidemiologic terms (Chapter 8). Nevertheless, toxicological experiments do indicate the kinds of physiological and pathological response of which animals and man are capable. Studies have been chosen for review in Chapters 5 to 7 on the basis of their possible relevance to air pollution problems, and the chapters are not comprehensive treatments of sulfur oxide toxicology.

While unreliable conversions and extrapolations are necessary in assessing health effects on man from toxicological experiments on animals, such experiments do, however, permit the use of higher concentrations, longer exposure times, larger numbers of subjects, surgical procedures, postmortem examinations, and other liberties not open to the experimenter with human subjects. Since man is an animal, the results of such animal experiments should have some relation to man, even though it is only qualitative. Therefore, this chapter deals with the toxicology of the oxides of sulfur in animals.

Methods of evaluation include exposing animals to the pollutant or pollutant combinations and examining mortality and changes in lung function that precede irreversible pathology. Absorption, distribution, and retention of sulfur oxides have also been examined, as have biochemical change and ciliary response in the organism. The effects of oxides of sulfur on animals have been reviewed by Setterstrom[1] and Negherbon.[2]

B. EVALUATION BY MORTALITY AND PATHOLOGY

1. Sulfur Dioxide Exposure

The response of various species including guinea pigs, mice, grasshoppers, and cockroaches to sulfur dioxide[1,3,4,5] has been studied. Concentrations from 30 to 3000 mg/m^3 (10 to 1000 ppm) were monitored and duplicate chambers were used for control animals.[6] Exposures were continuous up to the time of death of 50 percent of the animals or until no progressive symptoms appeared after considerable time. At concentrations of about 72 mg/m^3 (25 ppm) no mortality was produced by treatment up to about 45 days. At concentrations of 430 mg/m^3 (150 ppm) and below, mice were more resistant than guinea pigs. For example, it required 847 hours to kill 50 percent of the mice at 430 mg/m^3, whereas 50 percent of the guinea pigs exposed to about 370 mg/m^3 (130 ppm) died in 154 hours. At concentrations of from about 860 to 3000 mg/m^3 (300 to 1000 ppm), mice were less resistant than guinea pigs. At levels of around 3000 mg/m^3, 50 percent of the mice died in about 4 hours whereas about 20 hours were needed to kill guinea pigs. The susceptibility of the two insect species approximated that of the mice. It is thus apparent that extrapolations from high to lower concentrations of such parameters as species sensitivity are frequently not reliable.

No significant mortality or signs of distress were noted among healthy animals exposed to concentrations of 94 mg/m^3 (33 ppm) or below.

Longer exposure was needed to cause mortality when the exposures were intermittent. Exercise increased susceptibility of guinea pigs exposed to 3000 mg/m^3 but had no effect at lower concentrations.

Symptoms produced by the higher concentrations included coughing, moderate dyspnea, rhinitis, lachrymation, conjuctivitis, abdominal distension, lethargy, weakness, and paralysis of the hind quarters. Pathologic changes included slight to moderate visceral congestion, slight to moderate pulmonary edema, and distension of the gall bladder and stomach. Higher concentrations produced hemorrhages of lungs and stomach and acute dilation of the right heart.

The mean survival time of mice, guinea pigs, and rats was measured as a means of evaluating the effect of pretreatment with histamine, or of adrenalectomy, on the toxicity of sulfur dioxide.[7] Concentrations in the range of 1700 to 14,000 mg/m^3 (600 to 5000 ppm) were used, presumably because it was the aim to kill normal animals within a convenient time interval. For normal animals the susceptibility was highest in mice, intermediate in guinea pigs and least in rats. At the concentrations used in these experiments, the relative susceptibility of mice and guinea pigs is in agreement with the earlier data of Weeden et al.[8] mentioned above. Histamine given by intraperitoneal injection at levels of 200 mg/kg of animal weight 10 minutes before exposure significantly decreased the survival time of rats and mice. Adrenalectomy in rats also reduced survival time.

The extent of changes in lung pathology and the amount of fluid in the alveoli were primarily dependent upon the exposure time. In normal animals, pulmonary edema and areas of consolidation were usually observed, while animals whose survival time had been reduced by pretreatment, exhibited bronchial obstruction. Two mechanisms of death were observed in guinea pigs. A portion of each test group succumbed rapidly when introduced into the sulfur dioxide atmosphere. Occlusion of the bronchioles and venous congestion with little or no fluid in the alveoli were pathological changes observed in these animals. Those animals which survived 2 to 4 hours showed fluid in the alveoli, distended bronchioles, and partially desquamated mucosal membranes.

Tanami et al.[9] noted that in many animal experiments the effect of the animal housing environment before and during experimental trials had been little considered. Further, the animals have been exposed intermittently. They conclude that, from histopathological changes noted in autopsy of animal lungs in such experiments, the separation of SO_2 effects from other environmental effects has been extremely difficult, particularly with SO_2 concentrations below 110 mg/m^3 (40 ppm).

In an attempt[9] to eliminate environmental effects, 42 germ-free Hartley guinea pigs delivered by caesarean section were divided into two groups. One group was reared in germ-free isolators with 110 mg/m^3 (40 ppm) SO_2 gas atmosphere. The other group (controls) were reared in germ-free isolators in normal atmosphere. The animals were sacrificed after 3, 5, 6, 7, 8, 10, 12, 13, 14, and 18 days. From the experimental data, the experimenters concluded that germ-free guinea pigs in an SO_2 atmosphere of 110 mg/m^3 experience the following pulmonary effects: In the early stage, marked congestion and hemorrhage occur in the lung tissue. In the later stage, diffuse or nodular thickening of the alveolar septa becomes conspicuous. Throughout the experiment it was observed that only small numbers of immigrant cells were found in the nodular lesions.

Goldring et al.[10] reported that 29,000 mg/m^3 (10,000 ppm) produced 100 percent mortality of Syrian hamsters within 8 to 10 minutes. Exposures to 9,300 mg/m^3 (3,250 ppm) for periods up to 1-1/2 hours produced 50 percent mortality within 24 hours. Exposures of 1,850 mg/m^3 (650 ppm) for 75 days did not produce significant histopathological changes in the pulmonary tree of hamsters. Sodium chloride aerosol was also present in all exposures. (See Chapter 7, and Air Quality Criteria for Particulate Matter, a companion document, for a discussion of synergistic effects.)

Battigelli[11] exposed five groups of hamsters to room air, graphite dust (1 mg/m^3), graphite plus SO_2, calcium sulfate dust (1 mg/m^3), and calcium sulfate dust plus SO_2 (8 mg/m^3 (3 ppm)) for from 2 to 12 weeks twelve hours per day. One pair of animals from each group was sacrificed weekly. The respiratory tissues revealed no evidence of pathological change. The alveolar wall showed no emphysematous changes, proliferation, thickening, pneumonia, or signs of bronchitis. It was concluded that pulmonary injury is unlikely in these rodents exposed to 8 mg/m^3 SO_2, either alone or in combination with the two dusts used, for durations of several weeks in consecutive sessions of 12 hours per day.

A limited number of swine were exposed to about 14, 29, 57, and 114 mg/m^3 (5, 10, 20, and 40 ppm) sulfur dioxide for 8 hours.[12] Symptoms at 11 mg/m^3 (5 ppm) were limited to slight eye irritation and excess salivation. At higher concentrations there was excess salivation, excess nasal secretion, and shallower, more rapid respiration during the first 4 hours, after which the symptoms abated. Twenty-four hours after exposure the lungs showed hemorrhage and emphysema. The changes were less marked in animals sacrificed a week after exposure. Two animals exposed to 108 mg/m^3 (40 ppm) and one animal exposed to 54 mg/m^3 (20 ppm) which were sacrificed 160 days after exposure, showed some areas of fibrosis, and the lungs were a darker color and less well inflated than in normal animals.

Reid[13] attempted to produce hypertrophy of the goblet cells and mucous glands of rats which would simulate chronic bronchitis. Initially, animals were exposed 5 hours a day, 5 days a week, to about 108 mg/m^3 (40 ppm) sulfur dioxide. Since no great change was found in the lungs after 3 months, the dose was increased to about 900 to 1,100 mg/m^3 (300 to 400 ppm), in order to produce the desired changes. There followed an increase in the number of mucus-secreting cells both in the main bronchi, where goblet cells are normally frequent, and in the fine peripheral airways from which they are normally absent. Excessive mucus was seen in the bronchial lumen, probably reflecting an increased number of mucus-secreting cells as well as greater secretory activity, associated with reduced ciliary activity leading to retention. The changes apparently were not mediated through infection, as pathogens were not more frequently found in the bronchi and lungs of animals exposed to the irritant than in the controls. Although infection may act as an irritant, these experiments indicate that it is by no means an essential factor in the development of excessive mucous cells characteristic of chronic bronchitis.

In one experiment, the reaction was great in all but 2 animals, whereas in another experiment only half the animals responded. At the time of the diminished responsiveness, however, the supplier had made an attempt to breed a strain of animals less susceptible to bronchiectasis. It is likely that there is considerable difference in response between strains.

The excess of goblet cells persisted for at least 3 months after exposure to the irritant had ceased, even in the absence of infection. Most of the goblet cells were distended with secretion, suggesting that they discharged less mucus than during the exposure. The cessation of irritant exposure seemed to arrest the increase in cells.

Basmadzhieva et al.[14] exposed 15 male albino rats to 0.15 mg/m^3 SO_2 + 1 mg/m^3 CO, and 15 rats to 0.5 mg/m^3 SO_2 + 6 mg/m^3 CO 16 hours daily for 90 days. They concluded that rats exposed to SO_2 and CO for long periods developed pathological changes in their parenchymatous organs and lymph nodes, with the degree depending on the concentration of the two gases. Changes were most pronounced in the lungs. Morphologic changes were less marked in rats which were given a one-month recovery period.

Dalhamm[15] studied the morphology of tracheal mucosa in rats following exposures for periods of 18 to 67 days to about 30 mg/m^3 (10 ppm) sulfur dioxide. Exposures were 6 hours a day for 5 days a week, and 3 hours on Saturday; there was no exposure on Sunday.

Severe morphologic changes of the epithelium and lamina propria were observed. The epithelial surface was irregular with deep crypts, probably produced by cell proliferation. Since the cilia lining these crypts could not contribute to transport of mucus, such changes were a probable cause of observed retarded mucus flow. The changes were present at 18 days as well as at 67 days, and they had not regressed 4 weeks after exposure in six animals examined at that time. Support is thus lent to Reid's finding[13] of slow reversibility. There was no alteration of the ciliary ultrastructure although the surrounding tissues including ciliary cells showed severe changes. There was more mucus in the trachea of exposed animals. In healthy rats the mucus blanket was about 5 micrometers thick and the secretion contained only a few cellular elements. After sulfur dioxide exposure the mucus blanket was 20 to 25 micrometers thick and the secretion appeared more compact and contained numerous elements such as shed cells and white blood cells. Since the trachea is the main site of absorption of sulfur dioxide, these changes are not surprising at 27 mg/m^3 (10 ppm).

Fraser and Battigelli[16] exposed four groups of Sprague-Dawley white albino rats to 1 mg/m^3 of colloidal graphite with a discrete mean particle size <1.0 micrometer for 56 and 109 days. Five animals per group were used; one group from the 56-day exposure and one group from the 109-day exposure were also exposed to 8 mg/m^3 (3 ppm) SO_2. The objective was to detect any difference in the disposition of dust deposited in the alveoli of animals exposed to the dust in the presence or absence of SO_2. Sections of lungs were examined microscopically and the ratio of dust laden cells to the total number of alveolar cells in the same field were obtained. No difference could be determined between animals exposed to SO_2 and dust and those exposed only to the dust. In addition there was no difference between animals exposed for 56 days and those exposed for 109 days.

Won and Ross[17] subjected Rhizobium meliloti 102F5 in aerosols to SO_2. They were relatively insensitive to SO_2; 200 $\mu g/m^3$ were required to affect viability. Moisture content was varied and it was noted that the bactericidal activity of SO_2 appeared to be greater at 95 percent relative humidity than at 50 percent. In normal air high relative humidity favors maximal aerosol stability. It was hypothesized that the higher water content may favor or accelerate the formation of H_2SO_3, which acid may be more toxic than SO_2 itself.

2. Sulfuric Acid Aerosol

Experimental studies which use mortality and pathology as the criteria of response by necessity employ animals and use concentrations far above those occurring in the atmosphere in order to produce observable effects. Data from such studies cannot be extrapolated to give practical guidance in setting safe levels for the air pollutants examined. Such studies, however, constitute the most usual initial steps in investigating the toxicology of a substance.

A considerable species difference has been observed among small laboratory animals exposed to sulfuric acid mist. Treon et al.[18] exposed small numbers of several species to sulfuric acid mist, 95 percent of which was below 2 micrometers in size (diameter). Concentrations ranged from 87 to 1,600 mg/m^3. In order of increasing sensitivity were rabbits, rats, mice, and guinea pigs. Guinea pigs died at exposure concentrations survived by the other species and they showed proportionately greater respiratory irritation and lung pathology at nonlethal concentrations than the other species studied. Mathur and Olmstread[19] likewise found that mice were more resistant to exposure to sulfuric acid than guinea pigs.

Amdur et al.[20] determined the 8-hour LC_{50} of sulfuric acid having a mass median diameter (MMD) of 1 micrometer. The 8-hour LC_{50} was 18 mg/m^3 for 1- to 2-month-old guinea pigs and 50 mg/m^3 for 18-month-old animals. Sulfuric acid mists of 2.7-micrometer MMD were more toxic than those of 0.8 micrometer and the latter particle sizes were more toxic at

0° C than at room temperature.[21] These data indicate that the age of the animal, particle size, and temperature are all variables in determining lethality. Amdur et al.[20] found that a level of 8 mg/m^3 produced no deaths in animals exposed for 8 or 72 hours. These data suggest that the lethal effect of sulfuric acid is more dependent upon the concentration than on the duration of acute exposure; if the concentration will not induce a degree of laryngeal and/or bronchial [illegible] sufficient to cause death, a limited extension of the exposure time [illegible] not result in death. The fact that percent mortality at concentrations sufficient to kill some of the animals was not increased by extension of exposure time, and that the animals which died did so early in the exposure, suggests that the animals able to withstand the effects of laryngeal and/or bronchial spasm will survive such exposures for at least limited extension of the exposure.

Other variables found to influence mortality were enhancement when sulfuric acid was in the presence of smoke,[21] and inhibition when aerosolized ammonium carbonate excess was present with sulfuric acid mist.[22] The former was attributed to an increased particle size resulting from the adsorption of the acid on the smoke particles. The latter was attributed to a chemical neutralization of the sulfuric acid irritancy effect.

Both Amdur et al.[20] and Pattle et al.[22] examined the gross and microscopic pathology of the lungs of exposed guinea pigs. The pathological findings were similar in the two investigations. Animals dying after short exposures of less than two hours showed grossly distended and emphysematous lungs with no other serious lesions.[22] The cause of death in these animals appeared to be asphyxia caused by bronchoconstriction and laryngeal spasm. Animals dying after longer exposures showed gross pathological lesions including capillary engorgement and hemorrhage.[20,22] It is suggested that these changes are mainly a sequel to the combined effects of anoxia and increased intrathoracic pressure caused by bronchoconstriction and laryngeal spasm.[22] Animals that survived the exposures showed spotty areas of old hemorrhage and some areas of consolidation, especially around the hilar regions. Such damage is caused by exposures which do not result in death during or following exposure, and is repaired only very slowly.

As was indicated above, Amdur et al.[20] reported that extending the exposure time to 72 hours did not increase the mortality beyond that which was observed in 8-hour exposures. The pathological examination of the lungs, however, showed that there was much greater damage resulting from the longer exposures. Thickening of the alveolar walls and areas of consolidation were observed in the lungs of animals exposed to 8 mg/m^3 for 8 hours ($C \times T = 64$ mg/m^3-hrs), while the damage to the lungs of animals exposed to this concentration for 72 hours ($C \times T = 576$ mg/m^3-hrs) was greatly enhanced. They postulated that sulfuric acid mist has two distinct toxic actions. It promotes laryngeal and bronchial spasm, which is the cause of immediate death. This action is related primarily to concentration and individual sensitivity. Sulfuric acid mist can also produce parenchymal lung damage [illegible] is more dependent upon total dosage. Pattle et al.[22] poin[illegible] that this latter effect is probably a direct irritant action of the acid mist deposited on the lung tissue and may be the mechanism by which the mist causes death in those animals more resistant than is the guinea pig to bronchial-laryngeal spasm. Also, it may account for much of the marked differences in mortality observed by early investigators.

Thomas et al.[23] exposed guinea pigs to sulfuric acid mist for longer periods, ranging from 18 to 140 days. Three particle sizes were used: 0.6, 0.9, and 9 micrometers. The concentrations used were up to 4 mg/m^3 except for occasional accidental higher exposures. The coarse particles produced lesions of the upper respiratory tract. These consisted of a slight edema of the larynx and trachea and a decrease in mucus in the major bronchi. The sulfuric acid consisting of 0.9-micrometer particles produced greater lung damage than either the 0.6- or 9-micrometer particles. The exposure of young animals to 0.9-micrometer sulfuric acid produced the following pathological picture: the lungs were slightly edematous and a rare capillary hemorrhage was noted. There was some increase in desquamated epithelial cells in the minor but not in the major bronchi. The epithelium appeared intact. Major and minor bronchi showed a reduced amount of mucus compared to controls. The authors conclude that the guinea pig can tolerate levels of about 2 mg/m^3 sulfuric acid for more than three months of continuous exposure with only minor effects.

Bushtueva[24,25] exposed guinea pigs to 2 mg/m^3 sulfuric acid mist of unspecified particle size for five days. The animals developed edema and thickening of alveolar walls. One to two week exposures to 1 mg/m^3 produced a slight catarrhal condition of the mucous membrane of the trachea and bronchi, and slightly defined but widely distributed interstitial proliferative processes accompanied by round lymphoid cell infiltration surrounding the blood vessels and bronchi. These latter changes seemed to be progressive as they were more highly developed 2 to 3 months after exposure. A concentration of 0.5 mg/m^3 produced only a slight "lung irritation."

From these studies it can be concluded that sulfuric acid is a respiratory irritant that when present in sufficient concentration will cause the death of exposed animals. The guinea pig is the most sensitive species among the common small laboratory animals and hence very useful for studying the irritant potential of low concentrations of sulfuric acid. The greater sensitivity of the guinea pig results from its greater susceptibility to bronchial and laryngeal spasm. Concentration is a more important factor than duration of exposure in producing death.

Sulfuric acid also causes lung pathology. In effective short exposures (up to 72 hrs), the degree of lung damage observed is related to concentration and time rather than to the concentration alone. Such damage is slow to repair. Concentrations below 2 mg/m^3 produce only minor lung damage in extended exposures (about 3 months), indicating that the C and T relationship observed in 8- and 72-hour exposures cannot be extrapolated dirctly to long-term effects of low concentrations.

There is a clear indication that the particle size of sulfuric acid mist is an important factor in determining its irritant potency. When the criterion is mortality resulting from an 8-hour exposure, a mist of larger particles (2.7 micrometers vs. 0.8 micrometers) was more toxic. When lung pathology resulting from long-term exposures was the criterion of response, the effect of 0.9- micrometer particles was greater than either 0.6- or 9-micrometer particles.

C. EVALUATION BY PULMONARY FUNCTION

1. Sulfur Dioxide Exposure

In a series of papers, Amdur and her coworkers have reported on the respiratory response of guinea pigs to various irritant air pollutants, among them sulfur dioxide. The methods employed in all these studies are documented in the original paper dealing with sulfur dioxide[26] and in a paper dealing with physiological methods of measurement.[27] The method has the advantage that the animal is unanesthetized and breathing spontaneously. The information obtained in these experiments is, however, limited in comparison with studies of irritant action using anesthetized larger species. The method is suitable for routine daily use by a carefully trained technician, and data on numbers of animals exposed only once to a specific irritant can readily be obtained. This eliminates the need for re-exposure following "recovery" which is necessary in complicated physiological experiments.

Amdur and her coworkers used a standard exposure time of 1 hour; thus the applicability to air pollution criteria would be in connection with the possible effects of short-term peak values. Although the animals were unanesthetized during the control and exposure period, an intrapleural catheter was used, and this was put in place with the animals under light ether anesthesia. Mead[28] used another method which measured flow resistance without the need for an intrapleural catheter to measure the resistance of guinea pigs before and after intubation, and found that the procedure had caused an increase. It was not determined whether this increase was caused by the presence of the catheter or by the recent exposure to ether.

The method yields information on pulmonary flow-resistance and compliance (a measure of the elastic behavior of the lungs),[26,29] as well as tidal volume, respiratory frequency, and minute volume. One-hour exposures produced statistically significant increases in resistance ranging from about 10 percent at 460 μg/m^3 (0.16 ppm) to about 265 percent at 2,390 mg/m^3 (835 ppm).[30] For most normal human subjects, an increase in resistance of 300 percent or less would have no marked physiological consequences.

After exposure was terminated, resistance decreased and at concentrations up to 290 mg/m^3 (100 ppm) it returned to preexposure levels in the course of an hour. Resistance was back to normal 2 hours after exposure to 860 mg/m^3 (300 ppm).[31] A decrease in respiratory frequency was observed, and it became statistically significant at concentrations above 72 mg/m^3 (25 ppm).

The pattern of response produced by sulfur dioxide is typical[29] of the response of the guinea pig to a group of respiratory irritants which includes acetic acid, formaldehyde, and droplets of sulfuric acid smaller than 1 micrometer. At levels of about 6 to 14 mg/m^3, the other irritants all evoked a greater response than did sulfur dioxide. For this group of irritants, increased flow resistance is the most sensitive indicator of response.

Pulmonary edema is a relatively minor factor in the pathology of sulfur dioxide and similar irritants (although it is important for ozone and oxides of nitrogen).[32] The patterns of pathological response may relate to the ability of the irritant to penetrate to peripheral areas of the lung. Penetration is an important factor, but is not the only explanation, since irritant aerosols, of a size expected to penetrate readily, produced the pattern typified by sulfur dioxide and aldehydes.[33]

Amdur and her coworkers also measured the response of guinea pigs breathing irritants through a tracheal cannula.[26,29,30] The response to a given concentration of sulfur dioxide was greater when the gas reached the lungs through a tracheal cannula at concentrations of about 6 mg/m^3 (2 ppm) and above. At concentrations near 1.1 to 1.4 mg/m^3 (0.4 to 0.5 ppm) the response was not altered by the tracheal cannula. This supports the data of Strandberg[34] indicating that low concentrations of sulfur dioxide are not efficiently removed by the upper respiratory tract.

Exposures of guinea pigs breathing normally and via a tracheal cannula to sulfur dioxide at about 14 to 29 mg/m^3 (5 to 10 ppm) are reported by Davis et al.[35] Exposures of normal animals produced increases in resistance and tidal volume and decreases in respiratory rate and minute volume. Insufficient data are given to evaluate the specific effects of the irritant. There were no changes in respiratory function in animals exposed via tracheal cannula. Such animals did, however, respond with a resistance increase to inhalation of histamine aerosol. The authors conclude that sulfur dioxide is without effect on the lung and the entire response seen in normal animals is due to an increase in resistance of the upper airways.

This interpretation may be questioned since the pulmonary function tracings show evidence of technical errors where flow and volume appear completely out of phase with the pressure tracing. The results are not in agreement with those of Amdur and Mead[26] and of Amdur[29] obtained on guinea pigs, nor with the results discussed below for other species.

Goldring et al.[36] used Syrian hamsters with experimentally produced emphysema to examine the role of SO_2 on the pathogenesis of chronic-obstructive lung disease. A total of 72 animals were used, half with experimentally induced emphysema. Control animals were taken from both groups. Experimental animals from both groups were exposed to 1750 mg/m^3 (650 ppm) SO_2 daily for four hours per day, five days per week. Nineteen to 74 exposures were made. First exposure to SO_2 produced lacrimation, coughing, nose scratching and movement but acclimation occurred in several days. Weights of SO_2 animals were quoted as significantly lower. The exposure to SO_2 alone produced no significant change in lung compliance at 40 to 60 percent of volume, or lung recoil at 20 to 60 percent of volume, but the lung recoil at 80 to 100 percent volume was significantly lower. These animals tended to develop mild inflamatory changes in the bronchial tree, but it had no effect on air-flow resistance. In the emphysematous animals, the group treated with SO_2 failed to show any additional increase of lung compliance or reduction of lung recoil. A significant number did, however, develop mild bronchitis. The conclusion is drawn that preexisting pulmonary emphysema may enhance the inflamatory response reaction to SO_2 but its influence on air-flow limitation is of minor significance.

In two experiments, Kahana and Aronovitch[37] exposed young male albino rats to SO_2. In the first, 10 rats were given single exposures of three-hour duration to mean concentrations of 1880 mg/m^3 (688 ppm) SO_2. Properties of the lungs were studied using volume pressure determinations during fluid and air filling of excised lungs to separate tissue and surface forces. No significant changes were observed during saline filling when compared with controls. However, a marked decrease in mean transpulmonary pressures was exhibited during air filling. In a multiple exposure, five rats were subjected to nine four-hour periods of SO_2 exposure at mean concentration of 970 mg/m^3 (358.9 ppm) over a three-week interval.

The multiple exposure results appear similar to the single exposure. Changes in surface properties were felt to be obscured by other factors in this group including difference in lung size between exposed and controls, airway obstruction resulting from SO_2, and possible pulmonary edema. It is suggested that the reduced transpulmonary pressures during air filling might be attributed to a reduction in surface tension caused by increased secretion at the alveolar surface.

Leong and MacFarland[38] exposed seven groups of ten rats weighing 190 to 210 grams to 110 to 2000 mg/m^3 (40 to 750 ppm) SO_2 for two hours. Percent retention of SO_2 during exposure, along with respiratory rate and minute volume, varied inversely with SO_2 concentration, while tidal volume varied directly. Percent retention decreased with duration of exposure as well. Histologic examination revealed positive correlation between pulmonary damage and SO_2 concentration. Analysis of the percent retention during the first minute exposure as a function of SO_2 concentration was separated into two phases or mechanisms which mediate the percent retention with respect to SO_2 concentration. The first was described as a fast physiologic response perhaps attributable to bronchoconstriction. The second mechanism is described as a slow pathological response (superimposed on the maximum physiologic response) possibly caused by accumulation of bronchial secretions and pulmonary edema which could interfere with the absorptive processes of gases in the lung.

Balchum et al.[39-42] exposed anesthetized dogs to sulfur dioxide by nose and mouth breathing and by means of a tracheal cannula. Concentrations ranged from about 3 to 400 mg/m^3 (1 to 140 ppm), and exposure periods were 20 to 40 minutes. The dogs were not breathing spontaneously, but were ventilated at constant stroke volume following a dose of intravenous nembutal sufficient to stop spontaneous respiration. This represents an unusually deep level of anesthesia. A decrease in compliance and an increase in resistance were found at all concentrations used. These alterations were also produced when only an isolated segment of trachea was exposed to sulfur dioxide.[39] The resistance change was greatest in animals breathing via a tracheal cannula, intermediate in those nose-breathing, and least in those dogs in which only a tracheal segment was exposed. The compliance changes, on the other hand, were of the same order of magnitude in all cases. The compliance changes were possibly caused by some extraneous influence and not by sulfur dioxide, since spontaneous compliance decreases are a common phenomenon in dogs lying on their backs during prolonged physiological experiments.[43]

Salem and Aviado[44] ventilated dogs by pump through a tracheal cannula and measured the "dynamic" pressure-volume characteristics of the lungs during exposures of 570 to 2400 mg/m^3 (200 to 850 ppm) sulfur dioxide for periods of 1 to 4 minutes. The changes that ensued were consistent with bronchoconstriction preceded and followed by bronchodilation. These changes were interpreted as protective measures leading to a reduction in the amount of sulfur dioxide absorbed via the pulmonary circulation. They also observed pulmonary vasoconstriction, increase in pulmonary arterial blood pressure, a depression of myocardial force of contraction accompanied by brachycardia, and systemic shock.

Yokoyama and Ishikawa[45] measured the effect of sulfur dioxide on the mechanical behavior of the lungs of dogs exposed to 140 to 1000 mg/m^3 (50 to 350 ppm) via a tracheal cannula. There was consistent increase, occasionally as much as tenfold, in flow resistance. There were no consistent changes in pulmonary compliance.

Frank and Speizer[46] compared the functional response of several levels of the respiratory system to inhaled sulfur dioxide. Dogs were lightly anesthetized and exposed by nose, by tracheal cannula, and by an isolated segment of trachea. Concentrations ranged from 20 to 660 mg/m^3 (7 to 230 ppm), and routine exposures were for 15 minutes. Intervals of at least 20 minutes were allowed between exposures, and no animal was exposed more than 4 times. In eight animals exposed by nose the nasal resistance was measured. At levels of 20 to 175 mg/m^3 (7 to 61 ppm), the nasal resistance increased in a manner roughly proportional to the concentration, and at concentrations above about 70 mg/m^3 (25 ppm) it became progressively greater with duration of exposure. One animal showed a reduction in nasal resistance in the first 2 exposures and an increase in the second 2 exposures. During recovery, which lasted 15 to 40 minutes, the values reverted partially or completely to control values. The authors speculate that these changes probably reflect mucosal swelling, increased secretion of mucus or both. The resistance of the larynx appeared to rise and fall about an equal number of times during exposure and recovery. A significant change in one direction or the other occurred in about 45 percent of the observations. During nose-breathing the resistance of the lungs rose and fell about an equal number of times and the direction of change was not related to concentration of gas nor to duration of exposure. About one-third of these changes were considered statistically significant. Significant changes in either direction occurred more frequently at higher concentrations. During recovery the lung resistance tended to increase above control levels. Compliance was only slightly lower during exposure. Minute ventilation fell owing to slight reduction in both tidal volume and respiratory frequency.

When exposure was by tracheal cannula, pulmonary flow resistance rose rapidly, reaching a peak within several minutes, and then decreased. Limiting the exposure to the larynx and upper trachea produced a much less pronounced increase in lung resistance.

Spiegelman et al.[47] studied the effect of SO_2 exposure on bronchial clearance of monodisperse ferric oxide particles in donkeys. Each donkey inhaled SO_2 through two 60-cm-long plastic tubes (0.95 cm I.D.) which were connected to the side part of a duct carrying the SO_2-air mixture. Within two minutes they were given a five-minute inhalation of an aerosol of 1.8-micrometer ferric oxide particles tagged with gold-198 or technetium sulfide (TC-99m.)

Eight to 12 clearance experiments were done on each donkey over a two-month period. Half the experiments were directly followed by SO_2 inhalations for 30 minutes at fixed concentrations that ranged from 73 to 1950 mg/m^3 (27 to 713 ppm). The SO_2 exposure had no observed effect on bronchial clearance at SO_2 concentrations below 810 mg/m^3 (300 ppm). At higher concentrations of 1500 to 1950 mg/m^3 (557 to 713 ppm), the average clearance time was increased by as much as a factor of six. There was a profuse mucus discharge from the nose when impaired clearance was observed; hence, part of the SO_2 effect on bronchial clearance may be due to excess mucus production.

2. Mechanism of Response

Basic information on the mechanism of response to irritants is important in the complex task of assessing the irritant potential of air pollution. This is the realm of the physiologist, who may, for example, experiment with the effects of an irritant material on nerve fibers, or with the specific blocking effect of drugs. Exposures are usually brief, sometimes only a single breath, and quite frequently the concentration is not specified, but can be assumed to be very high.

Widdicombe[48] studied, in cats, the cough reflex elicited by mechanical stimulation, powdered talc or starch, and sulfur dioxide. He found that sulfur dioxide elicited the cough reflex when given through an endobronchial catheter so that the gas came in contact only with the lungs and smaller bronchi, and not with the trachea and extrapulmonary bronchi. The cough reflex produced in this way was always stronger than when the gas was applied to the trachea and main bronchi alone. After several inhalations of sulfur dioxide the cats became completely refractory to the gas but gave normal responses to mechanical stimulation of the trachea. This result suggested that the receptors sensitive to mechanical stimuli were not being stimulated by sulfur dioxide. Further evidence that the two receptors were distinct was provided by the fact that procaine solution sprayed into the trachea blocked the mechanical cough reflex but did not affect the response to sulfur dioxide.

Widdicombe[49] also made a systematic examination of different nerve endings in the tracheobronchial tree. One hundred single vagal fibers, which were excited by inflation of the lungs, were dissected, and the response was studied under various conditions. One group of these fibers was first sensitized, then inhibited, by sulfur dioxide. This particular group of fibers was distributed throughout the lower trachea and main bronchi. The responses of these fibers were not inhibited by procaine; this result parallels the observation that the cough reflex elicited by sulfur dioxide is not inhibited by procaine.[30] Another group of fibers was sensitive to mechanical stimuli but insensitive to sulfur dioxide; this sensitivity parallels the finding[30] that the mechanical cough reflex was still present in animals rendered refractory to sulfur dioxide. Vagal temperatures of 7° to 10° C blocked the fibers sensitive to sulfur dioxide. As with mechanical stimuli, sulfur dioxide acts via the sympathetic nervous system as well as the vagus nerves, and the group of fibers sensitive to sulfur dioxide has been shown to connect with the sympathetic trunk.

The mechanism of bronchoconstriction produced by sulfur dioxide in cats was also examined.[50] The animals were anesthetized, the respiratory muscles were paralyzed with gallamine triethiodide, and the animals were ventilated with a pump via a tracheal cannula. Sulfur dioxide was delivered either to the lungs or to the upper airways. Total pulmonary resistance was measured. Sulfur dioxide delivered to the lower airways and lungs during a single inflation cycle produced an increase in resistance which began during the first breath after exposure and returned to control levels within 1 minute. Exposing only the upper airways also produced a resistance increase. During cooling of the cervical vagosympathetic nerves the response was abolished whether the sulfur dioxide was delivered to the lung or to the upper airways. After rewarming of the nerves, the response was reestablished. The response was also abolished by the intravenous injection of atropine. The rapidity of the response and its reversal suggests that changes in smooth muscle tone are the cause of the bronchoconstriction. This response depends upon intact motor parasympathetic pathways. Similar results were reported by Widdecombe et al.[49,51] for bronchoconstriction caused by inhalation of fine charcoal dust.

3. Sulfuric Acid and Particulate Sulfate Exposures

Cho et al.[52] studied the mechanisms responsible for bronchoconstriction resulting from SO_2 and from cigarette smoke. Eight mongrel dogs were prepared so as to permit separate ventilation of the lower lobe of the left and right lungs. Bronchomotor response was recorded by measuring ventilatory overflow (increase corresponds to bronchoconstriction and decrease corresponds to bronchodilation). Blood pressure was measured at a variety of points to determine vasomotor responses. Inhalation of 0.01 to 1.0 percent SO_2 initiated bronchoconstriction in all the anesthetized dogs. The following observations were made: (1) Bronchoconstriction was in nearly all instances limited to the lobes exposed to SO_2 and did not occur in the lobes free of SO_2, eliminating an interlobar reflex. (2) Acute vagotomy followed by atrophine injection in two dogs and chronic denervation in two others did not affect bronchoconstriction, indicating that the vagus nerve system was not essential to bronchoconstriction.

(3) Exposure of the perfused lobe to SO_2 did not cause an elevation of the perfusion, excluding bronchomotor influence resulting from primary vascular response. (4) In three preparations, including perfusion of the right bronchial artery, SO_2 caused a fall in bronchial arterial perfusion pressure. One of the dogs had undergone vagotomy and injection of hexamethonium chloride, and the other two, chronic denervation. The bronchial arterial response was without change in pressure in pulmonary blood vessels and the heart; thus the effect was attributed to a primary response of the bronchial blood vessels.

Methods such as those discussed in this section permit the evaluation of response to concentrations of irritants at levels below those required to produce lung pathology or death. With such methods it is possible to examine the response of experimental animals to concentrations of air pollutants which are known to occur in urban atmospheres.

Amdur and Mead,[26,27] employing unanesthetized and spontaneously breathing guinea pigs, measured the following pulmonary function parameters: flow-resistance of the lungs and airways, compliance (a measure of the elastic behavior of the lungs), tidal volume (the volume of each breath), respiratory frequency, and minute volume. The data obtained also permit a rough estimate of the elastic, resistive, and total work of breathing.

The above methods were used to study the respiratory response of guinea pigs to sulfuric acid mist.[53] Concentrations ranged from 2 to 40 mg/m^3. Three particle sizes were used--0.8, 2.5, and 7 micrometers MMD. The experimental results indicated that the particle size of the aerosol is a very critical factor in determining both the nature and degree of irritant response. It also became clear from the results of these experiments that data obtained on high concentrations alone could not have been extrapolated to lower concentrations to yield valid information in regard to the relative irritant potency of different particle sizes of sulfuric acid mist. This fact underlines the need for and importance of methods which can assess directly the response to low concentrations of irritants.

The 7-micrometer particles at a concentration of 30 mg/m^3 produced a statistically significant increase in flow resistance but no other detectable changes in respiration. Particles of this size would not be expected to penetrate to any extent beyond the nasal passages. The increase observed in flow resistance very likely was entirely in the upper respiratory tract, especially as it was accompanied by no alteration in any of the other parameters measured.

The 0.8-micrometer particles produced an increase in resistance accompanied by a proportionally lesser decrease in compliance and an increase in elastic, resistive, and total work of breathing. These changes were statistically significant at the lowest concentration (1.9 mg/m^3) tested. The response was prompt in onset and resembled the pattern of changes observed in response to inhalation of sulfur dioxide. These findings are consistent with the narrowing of air passages within the lung either from bronchoconstriction or from mucosal swelling or increased secretion.

The 2.5-micrometer particles also produced an increase in flow-resistance at all concentrations examined from 2.3 to 44 mg/m^3. The relative toxicity of the 0.8- and 2.5-micrometer particles, as evaluated by resistance increase produced, was highly dependent upon concentration. At high concentrations the larger particles give a much greater response; whereas at low concentrations the smaller particles give the greater response. Thus, data obtained using only high concentrations would fail to predict accurately the response to low concentrations. The finding of a greater toxicity of the 2.5-micrometer particles compared to 0.8-micrometer particles at high concentrations confirms the finding of Pattle et al.[22] using the LC_{50} as the criterion of response.

A further comparison of the data for the two particle sizes indicated a difference in physiological action, presumably related to the site of deposition of the particles in the respiratory system. The response to the 2.5-micrometer particles was slow to develop, occurring only after 40 to 45 minutes of exposure. In animals exposed to the 2.5-micrometer particles, the delayed response suggested the possibility of a different mechanism of response, and this possibility was confirmed both by the nature of the changes in the mechanical properties and by the post-mortem appearance of the lungs.

Alterations in mechanical properties of the lung indicated that large sulfuric acid particles produced a complete rather than partial obstruction of some air passages, whereas small sulfuric acid particles caused a narrowing of the airways rather than complete obstruction. The gross pathology of the lungs was consistent with the data derived from pulmonary function tests. In animals exposed to the high concentration of 2.5-micrometer particles, there were extensive areas of atelectasis, frequently involving whole lobes. In addition, the lungs were edematous, as demonstrated by a significant increase in lung weight to body weight ratio. These findings suggest that with high concentrations of larger particles, which are probably deposited at the approximate level of the major bronchi, local irritation of the larger air passages causes swelling and increased exudation of fluid leading eventually to complete obstruction.

The resistance values were slow to return to preexposure values after the end of the 1-hour exposure. Animals exposed to 15 mg/m^3 and above still showed elevated resistance values two hours after the end of exposure. This slow return to normal has been a consistent finding in exposure to irritant aerosols or to the combination of irritant gas and inert particulate material.[31,54] The reasonable explanation for the slower recovery from exposure to an aerosol as compared to exposure to an irritant gas appears to be the fact that the particles, having been deposited on the respiratory tract, continue to exert their irritant effect. The irritant gases, on the other hand, are cleared from the lung when exposure ceases and the respiratory system returns to normal functioning rather rapidly, unless the exposure had been to an extremely high concentration. The enhancing effect of combining inert aerosols and irritant gases appears to be mediated through the formation of an irritant aerosol,[31,54] which can account for the prolonged response in such exposures.

Lewis et al.[55,56] studied the effects of chronic H_2SO_4 aerosol exposure on canine pulmonary function. Animals were exposed for 621 days and pulmonary function tests were performed following 221 days and 621 days of exposure to 0.5-micrometer H_2SO_4 particles at a concentration 0.8 mg/m^3. Exposure to this pollutant for 225 days resulted in a decreased diffusion capacity. After 621 days of exposure, average CO diffusion capacity, residual lung volume, and net lung volume following sacrifice were reduced; whereas total pulmonary resistance was increased.

Amdur and Corn[33] studied the irritant potency of zinc ammonium sulfate, zinc sulfate, and ammonium sulfate. They found a difference in the potencies of these compounds as judged by increases in flow-resistance from exposure to 1 mg/m^3 concentrations with a particle size of 0.29 micrometer.

Zinc sulfate exhibited about half the irritant potency of zinc ammonium sulfate. Ammonium sulfate was the least irritant of the three compounds, producing a response about one-third to one-fourth that observed from an equal concentration of zinc ammonium sulfate.

Further studies were made of the effect of particle size on the irritant potency of zinc ammonium sulfate. Four sizes were used: 0.29, 0.51, 0.84, and 1.4 micrometers. Concentrations ranged from 0.25 to 3.6 mg/m^3. Figure 5-1 shows the results obtained when the concentration of aerosol was held constant at about 1 mg/m^3 and the particle size was varied. It is evident that the irritant potency, as judged by the increase in flow resistance produced by the one-hour exposure, increased as the particle size decreased over the range of sizes examined. Amdur feels that the greater irritant potency of the smaller particles could be caused by an increase in the number of pinpoint stimuli resulting from the greater number of particles present in the more finely dispersed material, or that it could be caused by differing depth of penetration into the peripheral areas of the lung, or by a combination of these factors.

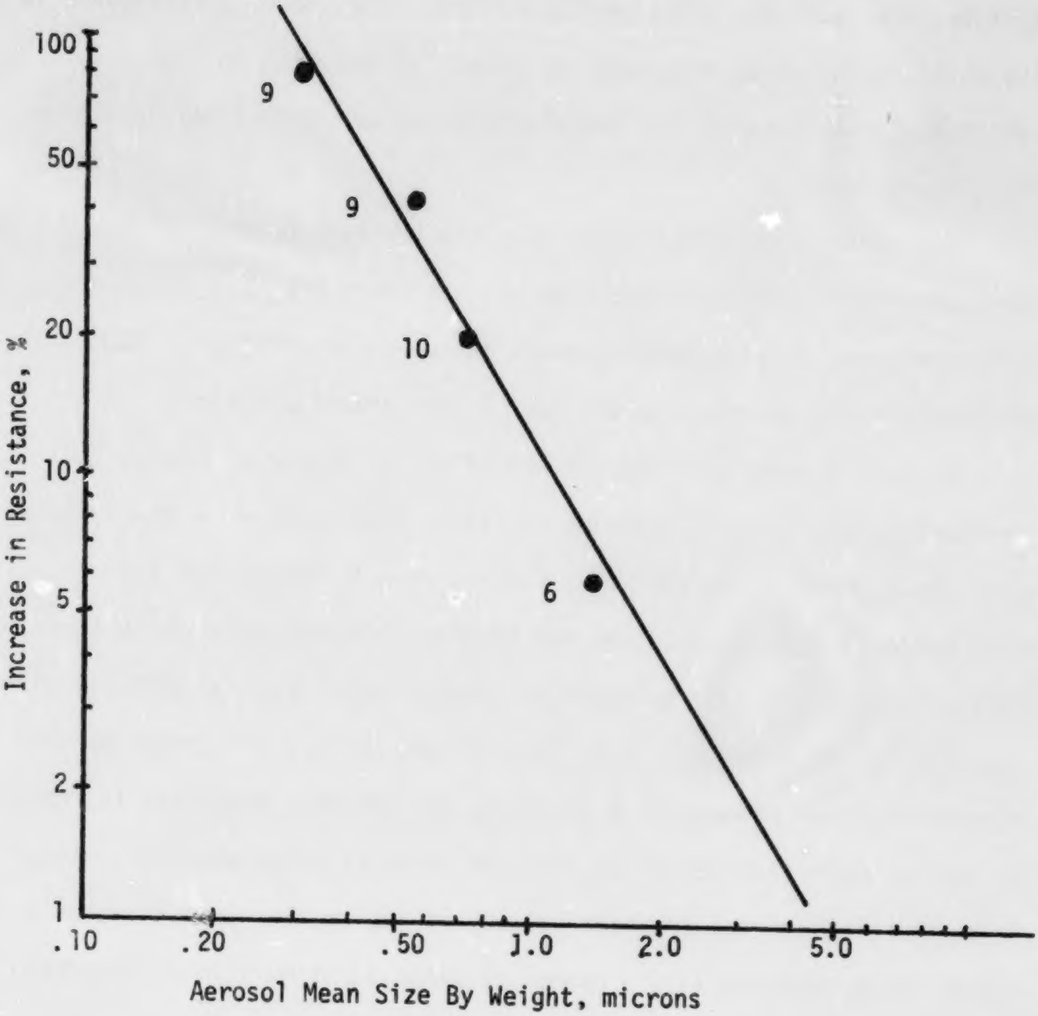

Figure 5-1. Effect of particle size on the response to approximately 1 mg/m^3 zinc ammonium sulfate. (Number beside each point indicates the number of animals. Data from Amdur and Corn.[33])

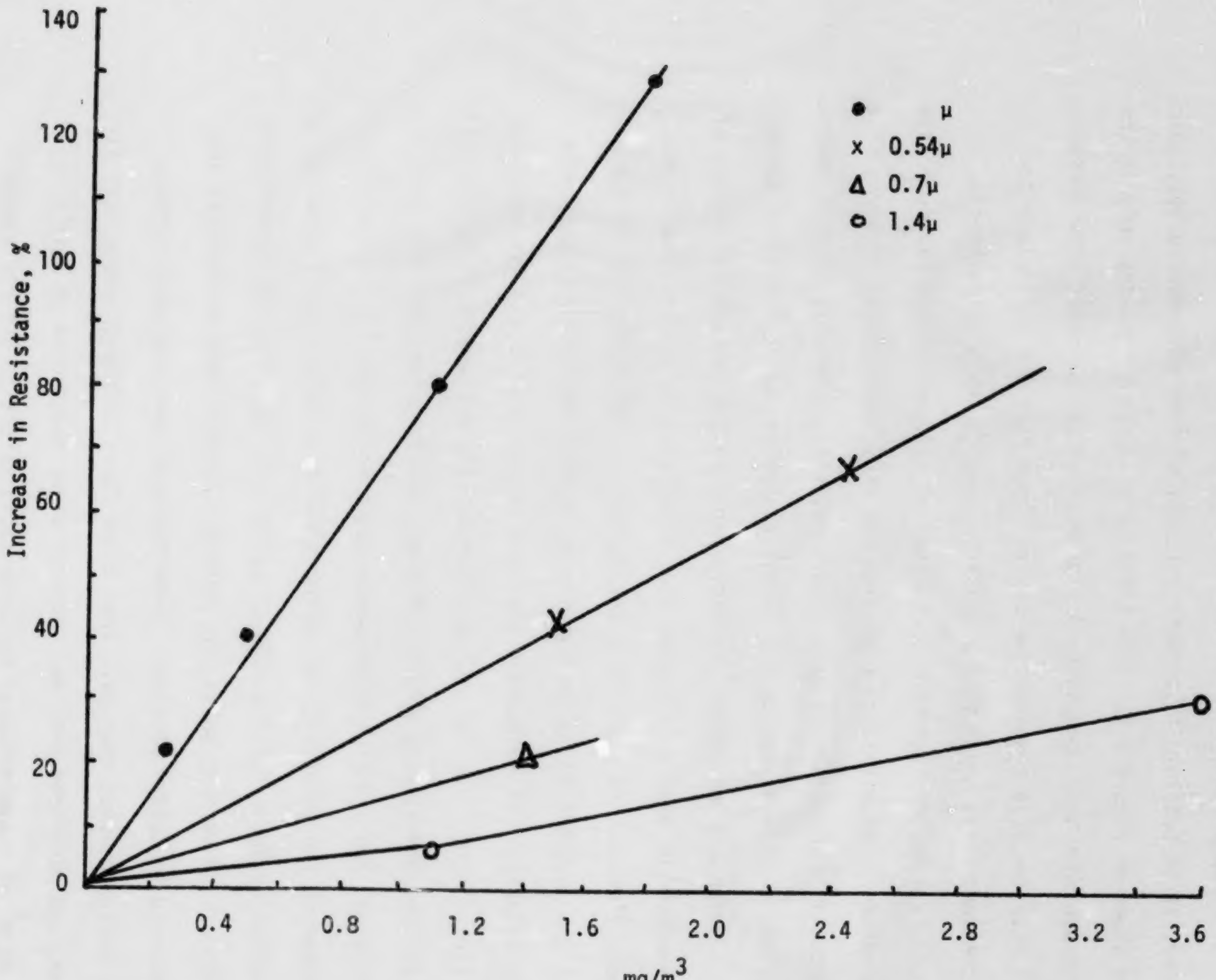

Figure 5-2. Dose-response curves for zinc ammonium sulfate of different particle sizes. (Number beside each point indicates number of animals. Data from Amdur and Corn.[33])

From data available for several concentrations at the various particle sizes, it is possible to prepare a family of dose-response curves, which are shown in Figure 5-2. From these it is evident that not only is the response to a given concentration greater as the particle size decreases, but also the dose-response curves are steeper as the particle size decreases. This means that a small increase in mass concentration produces a larger increment in biological response as the particle size decreases. These results emphasize the very important point that, if a compound is dispersed as particulate material, a measure of mass concentration alone does not permit useful assessment of its irritant potency.

Amdur and Underhill[57] recently reported the results of studies of the effect of various aerosols on the response to sulfur dioxide gas. Their findings indicated that the factors of importance in whether or not the response to sulfur dioxide as potentiated by an aerosol were the solubility of sulfur dioxide in a liquid droplet and its oxidation to sulfuric acid. The importance of solubility was suggested by the fact that the potentiating ability of aerosols of sodium chloride, potassium chloride, and ammonium thiocyanate could be related in a reasonable manner to the solubility of sulfur dioxide in solutions of these salts. Further evidence for the role of solubility came from the observation that of the various solid, dry aerosols tested, none potentiates the response to sulfur dioxide. These included spectrographic carbon, activated coconut charcoal, iron oxide fume, triphenyl phosphate, fly ash, and manganese dioxide. None of these substances at levels of 8 mg/m^3 or above produced any detectable effect on the resistance or potentiated the response to levels of sulfur dioxide ranging from 3 to 300 mg/m^3 (1 to 100 ppm). In contrast, aerosols of soluble salts of ferrous iron, manganese, or vanadium when used at concentrations of

0.7 to 1 mg/m^3 produced about a three-fold potentiation in the response to sulfur dioxide. These substances at significant humidity levels (as in the respiratory tract), would not only form droplets but also permit solution of sulfur dioxide; they are also known to be agents which favor the oxidation of sulfur dioxide to the more potent sulfuric acid. The properties of these and other sulfur compounds have been studied in depth by many researchers, and it has been found that the toxicity of the compounds is directly related to the metal ion itself rather than the attached sulfur radical.

Nadel et al.[58] studied the effects of aerosols of histamine and zinc ammonium sulfate aerosols on anesthetized, artificially ventilated cats. The aerosol was submicrometer in size and the concentration of zinc ammonium sulfate was 40 to 50 mg/m^3. The sulfate aerosol produced a physiological response similar to that of histamine but lesser in degree. The response to a 3-minute inhalation included increased pulmonary resistance, decreased pulmonary compliance, and increased end-expiratory transpulmonary pressure. To correlate with the physiological studies, anatomical studies were made after rapid freezing of the lungs in the open chest. These showed that the principal sites of constriction were the alveolar ducts and terminal bronchioles. Bronchioles up to 400 micrometers were narrower than in control animals and showed longitudinal furrowing of the mucosa. Bronchi and bronchioles larger than 400 micrometers were not significantly different from controls. The authors note the similarity in action of histamine and zinc ammonium sulfate aerosol. In regard to extrapolation of the results, the authors conclude, "It remains to be demonstrated that acute changes reported here at aerosol concentrations of 40-50 mg/m^3 are exaggerated but similar in nature to those produced, if any, at lower concentrations." Followup work is needed in this field.

In the course of examining the effect of aerosols on the response to sulfur dioxide, Amdur and Underhill[57] examined the irritant potency of several other sulfates. They report that ferric sulfate at 1 mg/m^3 produced a 77 percent increase in flow resistance in a one-hour exposure, which would definitely classify this substance as an irritant. On the other hand, ferrous sulfate and manganous sulfate at such a concentration produced no detectable alteration in resistance. Thus, not all sulfates are irritant in nature, indicating that the irritant potency may not always be related to the sulfate ion per se.

Since data from atmospheric chemistry have indicated that sulfuric acid and particulate sulfates are formed from sulfur dioxide emitted to the atmosphere, it is essential to examine the comparative irritant potency of the sulfur dioxide gas and its chemical reaction products. The long-term research program of Amdur[59] has provided data on both sulfur dioxide gas and on several particulate oxidation products studied by the same physiological techniques in the guinea pig, permitting a direct comparison of the irritant potency of these compounds. These comparative data, which will shortly appear in print, are summarized in Figure 5-3.

The evidence indicates clearly that an equivalent amount of sulfur present as sulfur dioxide gas produces a lesser irritant response than do the particulate sulfates or sulfuric acid. One part per million of sulfur dioxide is the equivalent of 1.3 mgS/m^3. When present as sulfur dioxide gas, this amount of sulfur produces an increase of about

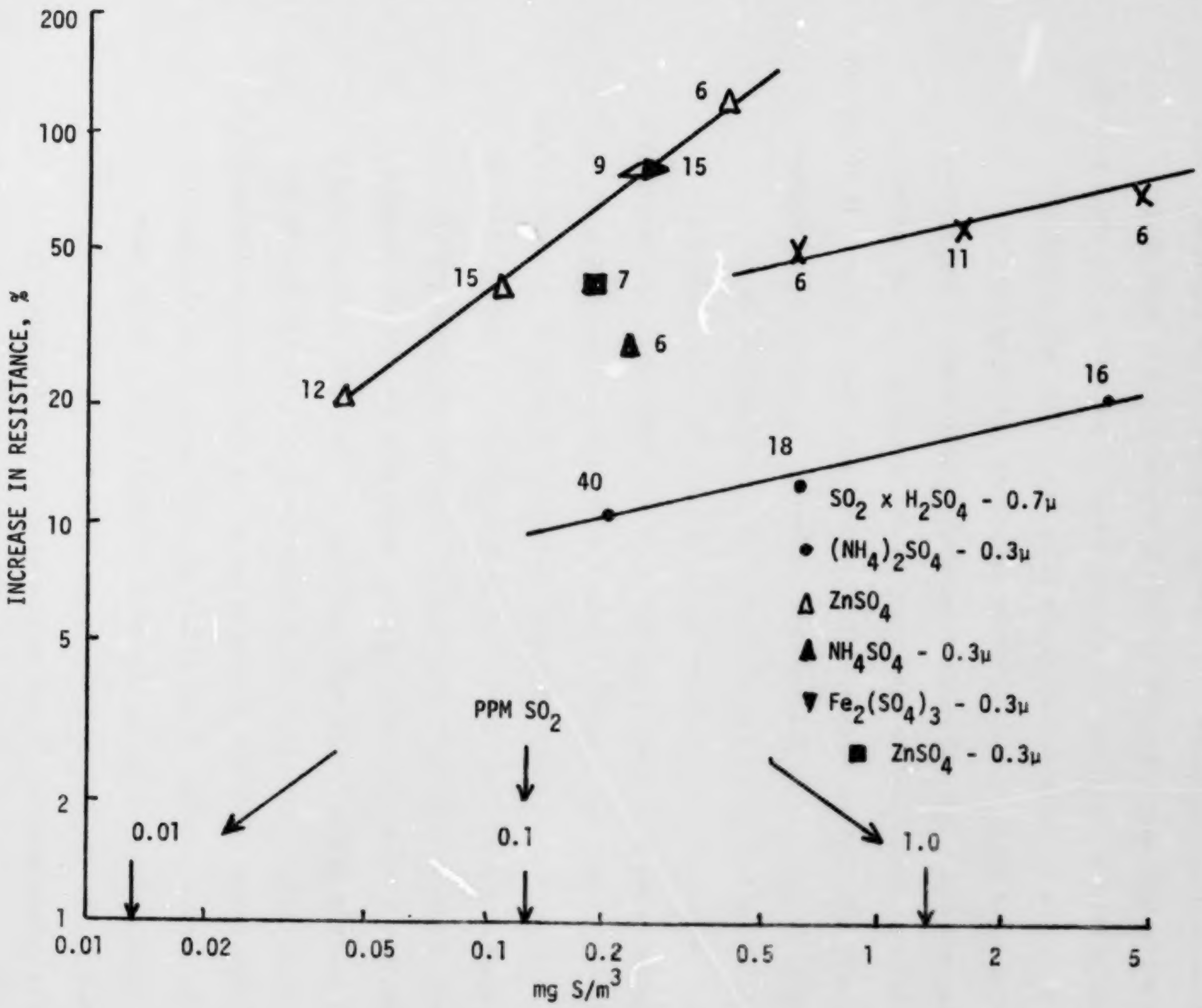

Figure 5-3. Comparative irritant potency of sulfur dioxide and sulfur-containing particulate material. (From Amdur.[59])

15 percent in flow resistance. If, through reaction in the atmosphere, this sulfur equivalent were converted to 0.7-micrometer sulfuric acid mist, it would produce a resistance increase of about 60 percent, a four-fold potentiation in irritant response. If on the other hand, that same amount of sulfur were converted to zinc ammonium sulfate of 0.3-micrometer, the response would be about 300 percent increase in resistance, a twenty-fold potentiation. Such complete conversion in the atmosphere is, of course, highly unlikely, but an oxidation of 10 percent can readily occur. If 10 percent of 3 mg/m^3 (1 ppm) sulfur dioxide were converted, it would give an equivalent sulfur content of 0.13 mg/m^3, and if this were present as an irritant sulfate of 0.3-micrometer particle size, it would produce a resistance increase of about 45 percent. If the response to the particulate sulfate formed and then 3 mg/m^3 (1 ppm) sulfur dioxide (which produced about a 15 percent increase) were purely additive, one could estimate a total resistance increase of 60 percent, an important four-fold potentiation in irritant response. There is evidence[33,60] that the response to such combinations is more than additive which would mean the overall irritant effect would be greater than indicated above. These data clearly suggest that toxicological evaluation of the response to only sulfur dioxide gas is not the proper basis for consideration of its role in air pollution.

The overall problem of the effect of inert aerosols on the response to irritant gases will not be discussed in detail here. It has been reviewed in the Air Quality Criteria Documents for both sulfur oxides,[61] and particulate material,[62] and is discussed in a review paper by Amdur.[63]

The studies discussed above cannot be extrapolated simply and directly to predict the response of man to these substances. However, they are useful in providing information regarding nature of effect mechanisms, and may well lend insight into responses in subjects who are more analogous to the sensitive segment of the population than to the robustly healthy. For practical considerations in using these experiments as indirect guidance in the area of air pollution, two points of critical importance emerge. The first is the extreme importance of the particle size on the irritant potency of particulate products of sulfur dioxide. Data on mass concentration alone is insufficient to predict irritant potency. The most important size range is at the level of submicrometer particles. The second important point is that the particulate oxidation products of sulfur dioxide are generally of a much greater irritant potency than the parent sulfur dioxide gas. It is thus critically important to assess atmospheric levels of sulfur dioxide and their health implications in terms of the potential for formation of more irritant substances. To do otherwise would miss the toxicological point or seriously becloud important issues.

D. EFFECTS OF SULFUR DIOXIDE ON CILIARY ACTION

Cralley[64] studied the effect of irritant gases, among them sulfur dioxide, on the ciliary activity of excised rabbit trachea. Temperature and humidity were controlled and the gas to be studied was passed over the tissue at a rate comparable to that of breathing by the animal. The time needed for cessation of ciliary activity following irritant exposure was related to the concentration of irritant administered. There was a rough correlation between the concentrations of sulfur dioxide needed to produce ciliary cessation in 10 minutes in the rabbit trachea (49 to 54 mg/m^3 (18 to 20 ppm)), and the values reported for concentrations causing immediate irritation of the throat in human subjects (22 to 32 mg/m^3 (8 to 12 ppm)).

The most extensive studies of the effect of sulfur dioxide and other irritant gases on ciliary activity of experimental animals have been made by Dahamn and his coworkers, using rats[15,65] and rabbits.[65-68]

The original work with rats[15,69] developed methods for measuring both rate of transport of mucus and the frequency of ciliary beat in the trachea of living animals under carefully controlled conditions of temperature and humidity. The action of sulfur dioxide on ciliary activity was tested at 140 mg/m^3, 70 mg/m^3, and 35 mg/m^3 (50 ppm, 25 ppm, and 12 ppm). The time required for cessation of ciliary beat varied with the concentration, being 50 seconds at 140 mg/m^3, 2 minutes at 70 mg/m^3, and 4 to 6 minutes at 35 mg/m^3. Rats which had been exposed to 30 mg/m^3 (10 ppm) for 48 days were examined for acute response to about 60 mg/m^3 (20 ppm) to compare their response with that of control rats not previously exposed. The results indicated that the previous exposure had not altered the reactivity of the cilia to the 60 mg/m^3 exposure. In all these experiments the cilia regained mobility a few minutes after exposure ceased.

There was a marked slowing of mucus transport and a complete cessation of flow in some rats exposed for 18 to 67 days to about 30 mg/m^3 (10 ppm). On the other hand, the rate of ciliary beat was slightly diminished in the shorter-term exposures and unaffected in the longer exposures. These findings were readily accounted for by the morphological changes which included a thickening of the mucus blanket from 5 to 25 micrometers and evidence of excess secretion. The rate of transport of mucus remained depressed in animals examined a month or so after the termination of exposure, in agreement with the persistence of the observed morphological changes.

Dalhamn studied the acute effect of sulfur dioxide on ciliary activity on the trachea of the rabbit in vivo and in vitro. The in vivo studies were made with the animals breathing spontaneously through the nose. Concentrations of the order of about 860 mg/m^3 (300 ppm) were required to produce cessation of ciliary beat in the spontaneously breathing rabbits. Obvious explanations for the contrast of this finding with the earlier findings on rats were either that the cilia of the rabbit trachea were relatively insensitive to sulfur dioxide or that the sulfur dioxide was not reaching the site of action. Experiments with the rabbit trachea in vitro showed that concentrations of sulfur dioxide of 20 to 29 mg/m^3 (7 to 10 ppm) were sufficient to produce cessation of ciliary activity. The absorption studies discussed below indicate that these findings are explicable on the basis of major absorption in the nasal cavity and pharynx of animals exposed via this route.

Fraser and Battigelli[16] exposed 24 Sprague-Dawley white albino rats to 3 mg/m^3 (1 ppm) SO_2 and 1 mg/m^3 of graphite dust (mean particle size <1.0 micrometer) for 5 hours per day, 5 days per week for a total of 20 days. At five-day intervals, 4, 4, 3, and 11 of the animals were examined. There were no obvious differences in ciliary beat between the exposed animals and the controls. Next, rats were again exposed to the same atmosphere but for 12 hours per day, seven days per week for four months. A total of 145 including controls were employed. Results were the same with no obvious difference between the control and exposed animals.

Battigelli[11] exposed five groups of hamsters to room air, graphite dust (1 mg/m^3), graphite plus 8 mg/m^3 (3 ppm) SO_2, calcium sulfate dust (1 mg/m^3) and calcium sulfate dust plus 8 mg/m$_3$ SO_2 for from 2 to 12 weeks, twelve hours per day. One pair of animals from each group was comparable at any interval of samplings up to completion of the three months of exposure. No ciliary effects due to dust, SO_2 or their combinations were observed.

E. LONG-TERM EXPOSURE OF ANIMALS TO SULFUR DIOXIDE

There are two brief reports[70,71] of a study in which rats were exposed over most of their lifetime to concentrations of about 3, 6, 11, 23, 46, and 92 mg/m^3 (1, 2, 4, 8, 16, and 32 ppm) sulfur dioxide. The life span of the rats appeared to be reduced by 0.08 months for each 3 mg/m^3 increase of sulfur dioxide concentration. Statistical analysis,[72] however, fails to attach significance to these changes.

Alarie et al.[73] undertook long-term continuous exposure of guinea pigs to SO_2 at concentrations ranging from 0.3 to 15 mg/m^3 (0.1 to 5 ppm). These values were chosen because they correspond to the lower end concentration encountered in urban atmosphere and to the upper end current threshold limit value established by the American Conference of Governmental Industrial Hygienists. Four groups of 120 Hartly albino guinea pigs (three experimental and one control group) were used. The three experimental groups were exposed to concentrations of 0.35 mg/m^3 (0.13 ppm), 2.8 mg/m^3 (1.0 ppm), and 16 mg/m^3 (5.7 ppm) for 22 hours a day, seven days a week for 52 weeks. Measurements were made on 10 males and 10 females selected by grab sample from each group before exposure, after three months exposure, and after 52 weeks exposure. Body weight, tidal volume, respiratory rate, minute volume, dynamic compliance, pulmonary flow resistance, work of breathing, hematocrit, hemoglobin, erythrocytes, leukocytes, blood urea nitrogen, and serum glutamic oxaloacetic transaminase determinations were made. Respiratory system flow resistance and CO uptake measurements were made on 10 males and 10 females from each group at beginning, every week for first four weeks, every three weeks until 28th week, and then every four weeks until 52nd week. Necropsies, in which the lungs, trachea, bronchial lymph nodes, heart, liver, and kidneys were microscopically examined, were made before exposure, after three months, and after 52 weeks of exposure. The pulmonary function measurements indicated that no detrimental changes could be attributed to the SO_2 exposure. The group exposed to 16 mg/m^3 SO_2 had much less variation in respiratory system flow resistance and a better diffusion index than the control group. Observations on lungs of animals exposed at 16 mg/m^3 concentration revealed an apparent reduction of incidence and severity of spontaneous pulmonary disease, and observations on the 16 mg/m^3 animals killed after 52 weeks exposure indicated a definite reduction in incidence and severity of spontaneous pulmonary disease. In the control and lower exposure groups there was a relatively high incidence of spontaneous pulmonary disease. Histiocytic infiltration was prevalent in all groups except the 16 mg/m^3. In the trachea submucosal infiltration of histiocytes and polymorphonuclear granulocytes were prevalent in all but the 16 mg/m^3 group. In addition there was a relatively high incidence of nephritis and nephrosis primarily in the males except in the 16 mg/m^3

group. Hepatocyte vacuolation increased in the liver of the 16 mg/m^3 (5.7 ppm) group. Finally, there was a significantly higher survival rate in males and females of the 16 mg/m^3 group as compared to the controls. The authors conclude that the guinea pigs were not adversely affected by the SO_2 exposures. They further conclude that both epidemiological studies and long-term studies in animals are requisite to the proper evaluation of environmental quality and voice the need for more long-term animal studies.

In a study of shorter duration Battigelli et al.[74] explored the surface microflora of 198 Sprague-Dawley rats. One group was exposed to 3 mg/m^3 (1 ppm) SO_2 and 1 mg/m^3 graphite dust, another group to 1 mg/m^3 graphite dust alone, and a third control group. Surface microflora from the turbinates, the stem bronchi, and the lung homogenates were monitored. In addition, histological studies of the respiratory structure, weight curves, and hematocrit were also obtained. Their preliminary analysis failed to indicate any trends which may be consistent with an SO_2 effect or any meaningful differences which could distinguish the animal groups.

F. ABSORPTION AND DISTRIBUTION OF SULFUR DIOXIDE

Balchum et al.[39,40,42] used labelled $S^{35}O_2$ to measure the absorption, distribution, and retention of sulfur dioxide in dogs. The effect of nose and mouth breathing as compared with breathing the gas through a tracheal cannula was examined, as well as the uptake and distribution following exposure of a segment of trachea only. Following inhalation, the sulfur dioxide was widely distributed to the tissues with obviously greater amounts in the respiratory tract. A smaller proportion of the inhaled gas was found in the trachea, lungs, hilar lymph nodes, liver, and spleen when the animals breathed through the nose and mouth than when the same amount was inhaled via a tracheal cannula. The labelled $S^{35}O_2$ was only slowly removed from the trachea and lungs, and its presence in these tissues could be detected a week after exposure. Ninety percent of inhaled sulfur dioxide was removed from the airstream and became localized in the respiratory tract including the pharynx. When a tracheal segment alone was exposed to the gas, S^{35} was detected in various tissues, indicating that it can be absorbed from the upper respiratory tract alone. S^{35} was detected in the urine but not in the feces.

Bystrova[75] found a wide distribution of S^{35} throughout the tissues of rats following inhalation of high concentraitons of sulfur (S^{35}) dioxide. The amount of S^{35} was attached to protein and could still be found 11 days after exposure. Traces, especially in the lungs, were detectable 3 weeks after exposure.

Frank et al.[76] exposed the surgically isolated airways of the head and upper neck of anesthetized, paralyzed dogs to 63 mg/m^3 (22 ppm) sulfur dioxide labelled with S^{35} and delivered at a rate of 3.5 l/min for 30 to 60 minutes. The trachea was cannulated below this region, and the lungs were ventilated with room air by a positive displacement pump. In 10 out of 12 measurements, over 95 percent of the sulfur dioxide administered to the isolated upper airways was found to be absorbed by the mucosa. In two of the animals, sampling was continued into the recovery period after the upper airways had been returned to room air, and sulfur dioxide was detected in one dog 5 to 37 minutes after exposure. In the other dog sulfur dioxide was present in the downstream sample 10 minutes after exposure but not at 60 minutes. The presence of sulfur dioxide was presumably due to desorption from the mucosa. In all 5 animals, sulfur dioxide was found in one or more expired gas samples collected either at the carina or from a bronchus. Since no sulfur dioxide entered the lower airways in inspired air, the authors conclude that the lungs were releasing the sulfur dioxide during expiration, presumably from the pulmonary capillaries. S^{35} appeared in the blood within 5 minutes of the start of exposure and continued to increase throughout the exposure. The radioactivity of the blood fell slowly during the 2-hour observation period following exposure; it was greater in the plasma than in the blood cells. Aeration of the venous blood sample caused a loss of about 20 percent of its radioactivity, but little or no radioactivity was lost by aeration of arterial blood. Radioactivity was also detected in the urine within minutes after exposure.

In a more recent paper Yokoyama et al.[77] investigated the interactions of S^{35} and blood and sought to identify the forms in which S^{35} is excreted in the urine. The surgically isolated airways of nine mongrel dogs were exposed: five to 64 mg/m^3 ±6 mg/m^3 (22 ±2 ppm) $S^{35}O_2$ and four to 145 mg/m^3 (50 ppm) $S^{35}O_2$. In addition the arterial blood of unexposed dogs and the venous blood of healthy volunteers were exposed to $S^{35}O_2$ in a tonometer at room temperature. The radioactivity of whole blood decreased little during post-exposure periods up to three hours in spite of continual renal excretion of S^{35} in the form of inorganic sulfate. The time required to transfer all S^{35} from the absorptive site is not known. In their experiments S^{35} was more concentrated in the plasma than in the red blood cells with more than one-half the plasma S^{35}

dialysable. Two-thirds of the S^{35} associated with the red blood cells appeared to be intracellular. Assuming all the $S^{35}O_2$ which entered the nasopharynx was taken up by the mucosa, then 1 to 6 percent of the S^{35} was excreted in the urine during the three hours of observation. The authors conclude that if the amounted excretion in the feces can be neglected, then the remaining 75 percent or more of the dose must have been distributed between the absorption site and the peripheral body tissues.

Dalhamn and coworkers[66-68] studied the absorptive capacity of the nasal cavity of rabbits for sulfur dioxide. Some animals breathed spontaneously through the nose from a chamber containing sulfur dioxide, and samples were taken from cannula inserted in the trachea immediately below the thyroid. In such animals, an initial exposure concentration of about 290 mg/m^3 (100 ppm) had been reduced to about 6 mg/m^3 (2 ppm) by the time it reached the tracheal sampling tube. A concentration of about 690 mg/m^3 (240 ppm) was reduced to about 6 to 9 mg/m^3 (2 to 3 ppm) by passage through the nasal cavity. During experiments in which air was pulled through the animal's mouth, the absorption was less. A concentration of 540 mg/m^3 (190 ppm) in the inhaled air reached the trachea at about 43 mg/m^3 (15 ppm). This observation fits with the observation by Speizer and Frank[78] that the increase in pulmonary flow resistance in human subjects was greater during mouth-breathing than during nose-breathing at a given concentration of sulfur dioxide in the inhaled air. Somewhat lower absorption values were obtained when air was sucked through the nasal cavity than had been obtained with the animals breathing spontaneously through the nose.

The overall conclusion is that at levels of 290 to 870 mg/m^3 (100 to 300 ppm), 90 percent or more of the inhaled sulfur dioxide does not reach the lungs. This offers a reasonable explanation for the high levels that are needed in experimental animals to produce lung pathology and mortality.

Strandberg[34] studied the absorption of sulfur dioxide by rabbits breathing spontaneously through the nose. A sampling device was implanted in the trachea, and the sulfur dioxide was tagged with S^{35} for analytical purposes. A concentration range of 145 $\mu g/m^3$ to 2,000 mg/m^3 (0.05 to 700 ppm) in the inhaled air was studied. There was considerable scatter in the data, but it was clear that at concentrations of about 290 mg/m^3 (100 ppm) there was an absorption of approximately 95 percent at inspiration and approximately 98 percent at expiration. As the concentration decreased, the absorption was less efficient, and at levels of 285 $\mu g/m^3$ (0.1 ppm) and below only about 40 percent was absorbed during inspiration and about 80 percent at expiration, with some experiments showing even lower absorption efficiencies. It was proposed that the higher concentrations cause excess secretion of mucus and increase the absorption efficiency.

Amdur[30] made use of Strandberg's data to replot the dose-response curve relating resistance increase to concentration of sulfur dioxide. The data on guinea pigs were available over the range of 460 $\mu g/m^3$ to 2,390 mg/m^3 (0.16 to 835 ppm), which was essentially the same range covered by Strandberg's studies. If the nasal absorption was 95 or 98 percent for high concentrations but only 40 or 50 percent for low concentrations as Strandberg observed, and if the response observed resulted from the concentration reaching the lung, this could perhaps explain the nonlinearity of the dose-response curve. When the air concentrations were calculated as effective "lung concentrations" using Strandberg's data, a straight line did result. At levels below about 290 mg/m^3 (100 ppm), the experimental curve for animals breathing through a tracheal cannula gave values quite close to the hypothetical "lung" curve. Strandberg's finding that, at low concentrations, sulfur dioxide penetrated the upper respiratory tract probably explains the similarity of response with and without the cannula at concentrations of 1.1 mg/m^3 (0.4 ppm). Strandberg's data obtained on rabbits appear to be applicable to guinea pigs.

G. MISCELLANEOUS BIOCHEMICAL EFFECTS OF SULFUR DIOXIDE

Not many experiments concerning the biochemical effects of SO_2 have been reported; those that have been reported are relatively scattered among various biochemical indices including reactivity with blood plasma and serum, effects on enzymes, and histamine release.

P'an and Jegier[79] recently investigated the effect of SO_2 on the enzyme acetylcholinesterase (ACRE) in vitro. ACRE was obtained from bovine erythrocytes type I. SO_2 was infused with a variable speed syringe and SO_2 concentration measured continuously. It was intended to work at SO_2 concentrations that can be found in ambient atmospheres, but in order to establish correlation between the degree of enzyme inhibition and the amount of SO_2 exposure, higher SO_2 concentrations were required. Threshold dose was 12 mg/m^3 (4 ppm) SO_2. From 18 mg/m^3 (6 ppm) upward relative enzyme activity versus SO_2 concentration gave exponential curves of the form $y = 100 - be^x$ where y is relative enzyme activity and x is SO_2 concentration. The authors concluded that, although in vitro studies cannot be directly extrapolated to in vivo experiments, the results obtained suggest that the bronchoconstriction induced by SO_2 in animal and man might be mediated by the action of SO_2 on ACRE.

Gunnison and Benton[80] investigated the reactivity of sulphite or bisulfite with mammalian plasma and serum under physiological conditions. Blood from the marginal ear vein of adult New Zealand rabbits was used for in vitro studies. In the in vivo tests two rabbits were exposed to 66 ±14 mg/m^3 (23 ±5 ppm) SO_2 for 14 hours and two others were exposed for 62 hours. It was concluded that sulfite which enters the bloodstream during exposure to atmospheric SO_2 forms S-sulfonate groups with constituents of the plasma. The reactivity of sulfite with plasma constituents is hypothesized as protecting many body tissues from high concentrations of sulfite and facilitating long-term exposure to very low levels of sulfite.

Basmadzhieva et al.[14] exposed 15 male albino rats to 0.15 mg/m^3 (0.05 ppm) SO_2 + 1 mg/m^3 (0.85 ppm) CO and 15 rats to 0.5 mg/m^3 (0.17 ppm) SO_2 + 6 mg/m^3 (4.2 ppm) CO 16 hours daily for 90 days. Exposure to the atmospheres affected the SH groups in the blood and serum with the higher pollutant level showing a statistically significant fall in the SH levels. Adrenal functions were disturbed as exhibited by a rise in vitamin C in the adrenals. Also, the cholinesterase level fell in both experimental groups in the first month; near the end of the third month and during the recovery period, it approached the level in the control group. The cholinesterase activity was interpreted by the authors as an index of the functional state of the nervous system.

Battigelli[11] exposed five groups of hamsters to room air, graphite dust, graphite plus SO_2, calcium sulfate dust, and calcium sulfate dust plus SO_2 for from 2 to 12 weeks, twelve hours per day at 8 mg/m^3 (3 ppm). One pair of animals from each group was sacrificed weekly. Hematocrit determinations, obtained from the common capillary tube, were very uniform among the five groups, leading to the conclusion that there were no significant effects of the various atmospheric exposures on this parameter.

Douglas et al.[81] were interested in the evidence that some effects of air pollutants are caused by release of histamine in lung tissue. They studied the effects of SO_2, NO_2, cigarette smoke, and histamine aerosols in spontaneously breathing guinea pigs. Exposure to SO_2 was for one hour at 100 mg/m^3 (34 ppm). The release of histamine by SO_2 was considered minimal and it was concluded that histamine release by air pollutants in guinea pigs is of minor importance.

Since experiments have demonstrated the wide distribution of S^{35} throughout the body following inhalation of sulfur dioxide, it is reasonable to search for possible biochemical effects. A biochemical lesion often is the fundamental basis for the response of an organism to toxic agents, and with many compounds the finding of such a biochemical lesion has provided the key to an understanding of their toxic action. There have been a few biochemical studies,[82-85] of animals exposed to sulfur dioxide, but from these no clear-cut picture of a biochemical lesion has emerged.

H. SUMMARY

This chapter describes animal toxicology of sulfur oxides. Both sulfur dioxide and sulfuric acid are considered in terms of dosage required to produce death, pathological change, and changes in pulmonary function. Both sulfur dioxide and sulfuric acid irritate the respiratory system; they must, however, be employed at high concentrations if mortality is chosen as the criterion of response. Sulfuric acid is more toxic than sulfur dioxide, and its toxicity is dependent on particle size. The guinea pig is apparently the most susceptible laboratory animal studied to date, although it can withstand concentrations of sulfuric acid which would be intolerable to man.

Compared to realistic air pollutant levels, it requires relatively high concentrations of sulfur dioxide or sulfuric acid to produce pathological lung change or mortality in animals. The type of pathological change observed in the guinea pig depends on whether the death was rapid as a result of bronchial spasm or was delayed.

Sulfur dioxide is capable of producing bronchoconstriction in experimental animals such as the guinea pig, the dog, the cat, and also in man. This bronchoconstrictive property is common to various respiratory irritants. Receptors in the tracheobronchial tree have been shown to be sensitive to sulfur dioxide and bronchoconstriction can be elicited by exposing only the upper airways to sulfur dioxide. The response is blocked by atropine or by cooling of the cervical vagosympathetic nerves.

Dose-response curves have been established for the guinea pig; they relate the concentration of sulfur dioxide to the observed increase in pulmonary flow resistance produced by one-hour exposures. Slight increases in resistance are detectable at 460 $\mu g/m^3$ (0.16 ppm) and the changes are readily reversible. The speed of onset (at least at high concentrations) and ready reversibility suggest that changes in smooth muscle tone are the cause of the observed bronchoconstriction.

Sulfuric acid and some, but not all, particulate sulfates also produce bronchoconstriction in the guinea pig. The response is highly dependent on particle size, with the smallest particles showing the greatest irritant potency. Comparative data are available only for the guinea pig; in this animal, sulfuric acid and irritant particulate sulfates have a greater irritant potency at a given concentration than sulfur dioxide alone.

Data obtained on guinea pigs suggest that the response to low concentrations is similar in type to that produced by higher concentrations but that the response decreases in magnitude with decreasing concentration. Indeed, in peak concentrations normally found in the urban environment, long-term exposure has not yet been demonstrated to adversely affect guinea pigs. The nature of the experimental techniques used on guinea pigs may render the animals especially sensitive to irritant action. Increases in flow-resistance produced in these animals are not considered as indications of major physiological change and are not suitable for direct extrapolation.

The physiological response elicited in cats by small particulate irritants is probably caused by reflex action on airway smooth muscle. Morphological studies show that the principal sites of constriction are the aveolar ducts and terminal bronchioles. Bronchi and bronchioles larger than 400 micrometers are unaffected. The response to the particulate irritants disappeared more slowly than did the response to gaseous irritants.

To summarize our knowledge of the absorption and distribution of sulfur dioxide, it has been shown that sulfur dioxide is absorbed in the upper airways, and nasal absorption can account for as much as 95 to 98 percent at high sulfur dioxide concentrations. This absorption provides a protective effect to the remainder of the pulmonary system and responses are generally greater when sulfur dioxide is breathes via tracheal cannulae.

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Chapter 6

TOXICOLOGICAL EFFECTS OF SULFUR OXIDES ON MAN

A. INTRODUCTION

Review of the health effects of air pollution have been made by Heimann,[1] Goldsmith,[2] Lawther et al.,[3] Phair,[4] Phillips,[5] Catcott,[6] Stokinger and Coffin,[7] and Anderson.[8] In addition, a number of shorter papersreport the health effects of polluted air which contains oxides of sulfur along with other pollutants.[9-27] These papers reveal the complexity of the problem of assessing the effects of air pollution. Anderson[8] states that although there are many serious limitations to pulbished research on the health hazards of air pollution, both epidemiological and detailed clinical, physiological, and animal experiments confirm that these hazards exist. He emphasizes the importance of particulate material as a major contributor to the noted responses, or as an index of air pollution related to these effects.

This chapter considers the available evidence, reported in the literature, on the toxicological effects of the oxides of sulfur on man. More extensive reviews of the toxicology of oxides of sulfur have been presented by Greenwald[28] and Amdur.[29] The combined effects of sulfur dioxide and particulate matter are discussed in Chapter 7.

Much of the human toxicological research has been oriented towards occupational health. Considerations affecting community air pollution must take account of the reactions of unusually sensitive individuals, so that the published studies are generally of limited applicability to the establishment of community air quality criteria.

B. EVALUATION BY PULMONARY FUNCTION

Various investigators have examined the response of human subjects exposed for brief periods to known concentrations of sulfur dioxide or sulfuric acid mist, and measured the effects on pulmonary function. The most valuable of these studies are those dealing with constriction of the airways as reflected in measurements of pulmonary flow resistance. Such experiments evaluate directly the response of man, thus having the advantage that extrapolation from the response of some other species of animal is avoided. On the other hand, the number of individuals used in these studies is necessarily limited, and a paper reporting the response of 10 subjects is considered a major contribution. It is difficult to extend results obtained on so limited a sample to define the response of any species of animals, and no one seriously proposes such extrapolations.

1. Sulfur Dioxide

a. Short-Term Exposures

Sim and Pattle[30] exposed healthy males aged 18 to 45 to sulfur dioxide either by face mask (264 exposures) for 10 minutes or in a chamber (330 exposures) for 60 minutes. During the chamber exposures the men were allowed to walk around or smoke if they wished. Mask exposures used concentrations from about 3 mg/m^3 to about 230 mg/m^3 (1 to 80 ppm), while concentrations in the chamber were from about 3 mg/m^3 to 65 mg/m^3 (1 to 23 ppm). The subjects were observed clinically, and increases in airway resistance greater than 20 percent were recorded.

From the wide range of concentrations, and the large number of exposures, a dose-response relationship was found. Unfortunately, it was not expressed in as much detail as the extensive experimental data warranted on this occasion. It was reported that with dosages below 800 mg-min/m^3 (equivalent to exposures of 10 minutes to 30 ppm or 60 minutes to 5 ppm) little change was noted either clinically or by measurement of lung resistance to air flow. Occasionally, there was an increase in lung resistance sufficient to be detected by the instrument used. At the same time, there were auscultatory signs of irritation in the chest of some, but not all, of the subjects. When dosages above 1330 mg-min/m^3 (presumably 50 ppm for 10 minutes or 9 ppm for 60 minutes) were used, the lung resistance increased significantly above normal in 50 percent of the people exposed. The authors did not define "significantly above normal" in this context. Measurements made during exposure showed that the increase of airway resistance occurred within the first 10 minutes with little further change at the end of an hour, which makes the authors' choice of the C and t-relationship to describe the pattern of response seem at variance with their findings. Rhinorrhea and lachrymation were common symptoms at higher dosages, but the most frequent physical finding was the presence of high-pitched musical rales, with a tendency to prolongation of the expiratory phase of respiration. Moist rales were commonly heard in the more peripheral regions of the lung after prolonged exposure, whereas in those who received smaller dosages or shorter exposures, rales were heard anteriorly over the large bronchi. Once again, this result seems at variance with the use of a C and t-relationship in connection with the data.

There was no correlation between familial history of allergy and symptomatology, but in isolated instances there was evidence of increased flow resistance and considerable discomfort in those who had previously been sensitive to fog in the London area or who had definite personal histories of allergy. The effect of the smoking habits of the subjects, or the effect of smoking during exposure, were not discussed.

In 8 out of the 594 exposures there were undefined "significant changes" in pulse rate, respiratory rate, volumes of tidal or supplemental air, vital capacity, maximum breathing capacity, or blood pressure. Two of these individuals had previous personal histories of allergy and two had experienced previous discomfort from smog. The other four were suffering from the onset of mild respiratory infections on the day of exposure. One person developed a unilateral, nonspecific pleural effusion one week after exposure. The investigators themselves were in normal health at the start of the experiments, which extended over a 10-month period. They both developed what appeared to be an increased sensitivity to sulfur dioxide and sulfuric acid mist. One of them, who was entirely free of chest symptoms at the outset, developed a moderately severe but extremely persistent bronchitis which was immediately exacerbated into an uncomfortable period of coughing and wheezing on exposure to either sulfur dioxide or sulfuric acid.

Frank and co-workers[31-34] have examined the response of human subjects to sulfur dioxide. In the experiments reported initially,[31] 11 healthy adults were exposed on separate occasions to average sulfur dioxide concentrations of about 3 mg/m^3 (1 ppm), about 14 mg/m^3 (5 ppm), and 37 mg/m^3 (13 ppm). Exposures lasted 10 to 30 minutes and, for each subject, were spaced at least one month apart. The subjects were seated in a body plethysmograph, breathing spontaneously by mouth while measurements of respiratory mechanics were made with an esophageal catheter. The measurements did not necessitate the interruption of exposure to the gas. At 3 mg/m^3 only one of the 11 subjects showed a statistically significant increase in flow resistance, and his control resistance was the highest encountered. One other subject showed a statistically significant decrease in resistance during exposure to 3 mg/m^3 (1 ppm). At the 14 mg/m^3 level, 9 out of the 11 subjects showed a statistically significant increase in resistance over control values, and the average increase for the group was 39 percent above control. At 37 mg/m^3 all subjects showed an increase in resistance, and 9 of these measurements were statistically significant on an individual basis. The average increase for the group was 72 percent above control.

The data obtained in man may be compared with data obtained by similar methods in guinea pigs exposed to the same concentrations. Data for guinea pigs were available for animals breathing normally and breathing through a tracheal cannula. The human subjects were mouth-breathing. It was found that, except at the lowest gas concentration, the human subjects appeared to be slightly more sensitive than the guinea pigs. The most comparable dose-response relationships were for the tracheotomized guinea pigs and the normal human subjects.

The time course of the resistance changes was examined. Within 1 minute of exposure, flow resistance had increased significantly. The increase after 5 minutes was greater than the increase at 1 minute, but no further significant change occurred between 5 and 10 minutes. If the 5- and 10-minute values are averaged to represent the "peak" response, then 45 percent of this peak was reached within the first minute of exposure. Five exposures to the higher two concentrations of 14 and 37 mg/m^3 (5 and 13 ppm) were extended to 30 minutes, but although the resistance remained elevated throughout this exposure period, the resistance tended to decrease slightly from the 10-minute values. (In this regard, the response of human subjects to sulfur dioxide differed from that of guinea pigs, in which the resistance did not decline during an exposure period of 1 hour[35,36] and continued to increase in a limited number of animals exposed for 3 hours). The extension of the exposure time to 30 minutes for 5 subjects exposed to 3 mg/m^3 (1 ppm) did not produce an increase in flow resistance, suggesting that, within the limited time intervals studied, the response is related to the concentration of sulfur dioxide and not to a C and t-relationship. This statement cannot obviously be extrapolated to long-term exposures.

The average flow resistance for the group still remained elevated 15 minutes after the end of exposure to both 14 and 37 mg/m^3 (5 and 13 ppm) sulfur dioxide. At 14 mg/m^3 the difference was statistically significant in 4 individual subjects; at 37 mg/m^3 it was not significant for any individual subject. In 5 subjects, periodic measurements were made within the 15-minute period and it was found that, at times, recovery may be completed within less than 5 minutes after exposure ceases. This point should be borne in mind when using techniques which involve a lapse of time between exposure and measurement.

A decrease in compliance was noted in only one single instance during an exposure to 37 mg/m^3 (13 ppm). At the same time the increase in flow resistance of this individual was below the average of the group. Once again the response of human subjects appears to differ from that of guinea pigs in which slight decreases in compliance appeared to accompany the resistance increase. There was a slight increase in functional residual capacity at 37 mg/m^3, but the two lower concentrations of 3 and 14 mg/m^3 (1 ppm and 5 ppm) produced no change. Alterations in maximum flow rate (as measured with the Wright peak flowmeter) and in timed vital capacity were minimal when compared to alterations in pulmonary flow resistance. Exposures which increased the pulmonary flow by 89 percent showed only a 7 percent decrease in peak flow and, though the timed vital capacity values were generally lower, the changes expressed as percentages were minimal. A possible explanation for the relative insensitivity of these measurements is that they are preceded by a maximal inspiratory effort which may temporarily obliterate changes of flow resistance of the magnitude of those seen in this study. The smoking habits of the subjects did not appear to influence the response to sulfur dioxide.

Snell and Luchsinger[37] have recently studied the acute effects of SO_2 (1.5 to 14 mg/m^3 (0.5 to 5 ppm)) both alone and in combination with saline and water aerosols. First, nine volunteers (five men and four women) with no significant history of pulmonary or allergic disease in the age range 20 to 40 were tested. Maximum expiratory flow from one-half vital capacity ($MEF_{50\%VC}$) was obtained in air. Then the subjects breathed through a mouthpiece (1) aerosols of distilled water and normal saline, (2) SO_2 in air at 1.5, 3, and 14 mg/m^3 (0.5, 1, and 5 ppm) (3) SO_2 at the same concentrations mixed with normal saline aerosol, and (4) SO_2 at the same concentrations mixed with distilled water aerosol. Before each challenge each subject breathed normal air from the apparatus. Each exposure to the various challenges was 15 minutes. $MEF_{50\%VC}$ was measured within 15 seconds of the end of each control and challenge period. In a second series, five subjects breathed one of three gas mixtures through a mouthpiece or mask: (1) 14 mg/m^3 SO_2 in air, (2) 1.5 mg/m^3 SO_2 in distilled water aerosol, and (3) 14 mg/m^3 SO_2 in distilled water aerosol. Exposure periods and $MEF_{50\%VC}$ measurements were conducted the same as in the first series. Total pulmonary resistance measurements were made at four-minute intervals. It should be noted that the saline aerosol produced a particle-size distribution with maximum number of particles in the 6- to 8-micrometer diameter range with no submicrometer particles while the distilled water aerosol particle size was in the submicrometer range.

For SO_2 in the air, $MEF_{50\%VC}$ decreases at the 3 and 14 mg/m^3 (1 and 5 ppm) exposures. For SO_2 with saline aerosol, $MEF_{50\%VC}$ decreased significantly for the 14 mg/m^3 exposure. For SO_2 with water aerosol, $MEF_{50\%VC}$ decreased significantly for all three SO_2 levels. Potentiation thus occurred for the water aerosol but not for the saline aerosol. The reason for this difference is attributed to the large particle size (6 to 8 micrometers) of the saline aerosol. It has been demonstrated in other experiments that synergism does not occur for particles above 2.5 micrometers in diameter because of the fact that nearly all of such large particle sized aerosols is retained in the upper respiratory tract.

The second series of measurements, which was designed to evaluate the difference in effect when SO_2 was inhaled through the nose rather than the mouth, $MEF_{50\%VC}$ was higher for nasal exposure and most prominent for the dry gas.

Burton et al.[38] investigated the synergistic effects of SO_2 plus aerosols on ten male volunteers by measuring airway resistance and pulmonary flow resistance at pollutant concentrations resembling those found in urban air. Control measurements were made and followed by 30 minute exposures to SO_2 or an SO_2 plus saline aerosol. Measurements were made at 10 and 30 minutes. Clearance time between exposures was sufficient to return to control values. Sodium chloride concentration in the aerosol was 2.2 ± 0.08 mg/m^3 and mean aerosol particle size was 0.25 micrometer ± 0.001 micrometer. SO_2 concentration varied from 3 to 9.7 mg/m^3 (1.1 to 3.6 ppm) for the various exposures. The study agreed with other evidence reported in the literature that human exposures to low concentrations (<9 mg/m^3) of SO_2 in air do not result in immediate physiologic effects on measures of pulmonary mechanics. Burton et al. were unable to demonstrate synergism for SO_2 plus inert aerosols at concentrations approaching those in urban atmospheres. These results are at variance with the conclusions reached by Snell and Luchsinger on human beings and by Amdur on animals. Burton et al. do not rule out the possibility of such synergism but feel that studies of changes in resting pulmonary mechanics may not be sensitive enough to reveal such changes. They suggest studies of pulmonary mechanics changes following exposure during exercises as possibly being more sensitive indicators.

b. Repeated Exposures

Frank et al.[34] also found that when sulfur dioxide (either with or without sodium chloride aerosol) is administered twice in the course of one experiment (with a 15-minute period of clean air between exposures), the response to the second exposure is less than the response to the first. The human subjects thus showed an adaptation to repeated exposure to the gas.

Speizer and Frank[33] compared the effect of sulfur dioxide on human subjects breathing the gas by nose and by mouth. Eight subjects were studied. Exposures were to either about 43 mg/m^3 (15 ppm) or about 80 mg/m^3 (28 ppm) sulfur dioxide and were of 10-minute duration. Pulmonary flow resistance was measured during both types of exposure. The flow resistance of the nose was measured during the nose breathing exposures. When sulfur dioxide was breathed by mouth the pulmonary flow resistance increased in 9 out of 12 experiments, and the magnitude of the change was on the average greater at the higher concentration. When the same concentrations of sulfur dioxide were administered by nose, pulmonary flow resistance increased in only 3 out of 12 experiments and decreased in one experiment. During the 15 minutes following the end of exposure, the resistance remained elevated in 5 out of 12 experiments in which the gas was breathed by mouth. Four of these exposures were to 80 mg/m^3. When the gas was breathed by nose, the pulmonary flow resistance was often higher during the recovery period than it had been during exposure. In 3 experiments it rose significantly for the first time during the recovery period, and in 2 others the increase was greater during recovery than it had been during exposure.

The response of nasal resistance to sulfur dioxide was variable.

In 8 of the 12 experiments it increased at some point during exposure; in 3 experiments there was a decrease; and 1 subject showed first a decrease and then an increase during the same exposure. The subjects who showed an increased nasal resistance experienced no difficulty in breathing.

When exposed by mouth, most of the subjects coughed several times during the first few minutes and had slight burning sensations of the throat and substernal area for at least 5 minutes. When exposed by nose, there was little coughing and no chest symptoms although some subjects did experience irritation of the posterior pharynx which lasted a few minutes.

Nadel et al.[39] reported that airway resistance, determined with a body plethysmograph, was increased by exposure to about 6 mg/m^3 (2 ppm) and about 14 mg/m^3 (5 ppm) sulfur dioxide for 3 to 10 minutes. One individual out of 7 exposed to 14 mg/m^3 for 10 minutes, showed a marked increase in airway resistance which was reversible by isoproterenol inhalation. This subject had no previous history of pulmonary disease. In later studies[40,41] an examination was made of the response of 7 subjects exposed by mouth for 10 minutes to from 12 to 17 mg/m^3 (4 to 6 ppm) sulfur dioxide. Such exposures increased the airway resistance, and the onset of change varied from 10 seconds to 4 minutes. A maximum response was usually observed within 1 minute, but in 2 subjects the resistance increased during continued exposure, and in 2 others the resistance decreased during exposure. The subject who showed the greatest change became dyspneic and wheezed during the exposure. After subcutaneous injection of 1.2 to 1.8 mg atropine sulfate, sulfur dioxide caused no significant change in airway resistance. Most subjects coughed and some experienced irritation of the pharynx and substernal area. These symptoms were not affected by the atropine.

Tomono[42] reported that the lowest level of sulfur dioxide which could induce broncho-constriction in 46 healthy male subjects was about 4.6 mg/m^3 (1.6 ppm). The changes were relieved by isoproterenerol inhalation.

Burton et al.[43] examined airway resistance and dynamic lung compliance in 10 subjects immediately following 30-minute exposures to about 3 to 9 mg/m (1 to 3 ppm) sulfur dioxide. Comparison with individual or mean group controls did not reveal significant increases in resistance or compliance during quiet breathing or during hyperventilation.

2. Sulfuric Acid Aerosol

In 1913, Dorsch[44] studied workers in the battery room of a German telephone exchange. The H_2SO_4 mist was only rarely detected by the employees when the concentration was below 0.5 mg/m^3. Slight irritation of the nose and throad was felt at 2 mg/m^3. Distinct discomfort at 3 to 4 mg/m^3 and marked discomfort was noted when the concentration rose to 6.8 mg H_2SO_4/m^3 air. Then, in 1957, Bushtueva[45] exposed ten volunteers to H_2SO_4 aerosol. At concentrations of less than 1.1 mg/m^3 there were complaints of throat tickling and scratching; all subjects noticed considerable irritation at the base of the esophagus and 40 percent experienced some irritation of the eye mucosa when the H_2SO_4 level was between 1.1 and 2.4 mg/m^3; and, when the aerosol level was raised to 2.4 to 6.0 mg/m^3, acute irritation of the mucous membranes, a pronounced reflex cough and irritationof the eye mucosa were present in all subjects.

The maximum concentration not detected by the subjects was found to be approximately 0.6 mg/m^3 (0.55 to 0.7 mg/m^3), while the minimum concentration sensed averaged 0.715 mg/m^3 (0.6 to 0.85 mg/m^3). The particle size of the acid mist was not stated.

In another study, Bushtueva[46] found that the presence of 0.4 mg. H_2SO_4/m^3 even when combined with 1 mg. SO_2/m^3 air was below the sensitivity threshold of all subjects. All of these papers are remarkably similar to Dorsch's[44] original description of H_2SO_4 mist irritancy. Thus, the dose-response curve in the human being has remained quite stable during the past sixty years of experimentation, and, in apparent contrast to animal data, is physiologically predictable in almost all instances.

Sim and Pattle[30] studied the response of healthy males aged 18 to 46 to H_2SO_4 mist noting that high humidity and temperature, low normality (N), and a large particle size were found to be more irritating than an aerosol of the same concentration with higher normality, lower humidity and temperature, and a smaller particle size. Pulmonary air-flow resistance was 35 to 100 percent greater than normal when they used a 10N H_2SO_4 aerosol of 1 micrometer MMD at a concentration of 39 mg. H_2SO_4/m^3 air at a temperature of 18.4° C and a humidity of 61 percent. Upon increasing the temperature to 25° C and humidity to 91 percent, a 4N H_2SO_4 mist with a MMD of 1.5 micrometer resulted in intense coughing, lacrimation and rhinorrhea which continued throughout the exposure. Coughing somewhat decreased after the first ten minutes of exposure and airway resistance ranged from 43 to 150 percent greater than normal at this time. Furthermore, the addition of magnesium oxide did not diminish the irritancy, although adding ammonia towards the end of the H_2SO_4 exposure resulted in rapid and complete disappearance of all symptoms. Toyama and Nakamura[47] also correlated airway resistance with particle size. Using a 4.6-micrometer aerosol, a mist concentration of 0.8 to 1.4 mg/m^3 increased airway resistance 36.5 percent in twenty-four healthy males; upon using a 1.8-micrometer particle at a concentration of 0.01 to 0.1 mg/m^3, airway resistance was increased 17.9 percent. The latter concentrations appear questionable since 0.01 to 0.1 mg. H_2SO_4/m^3 air are levels far below those reported as capable of producing any physiological response.

Hamilton and Hardy[48] in 1948, stated that the action of H_2SO_4 fumes is on the upper respiratory tract and "... that this action is not severe, and that there is no instance of bronchitis ... traceable to such fumes." However, Sim[30] described how he himself became increasingly sensitive to the mist during ten months of exposure, developing a moderately severe, but extremely persistent bronchitis which was immediately exacerbated into an uncomfortable period of coughing and wheezing upon exposure to H_2SO_4 mist.

An apparent increase in the respiratory rate of all human subjects exposed to H_2SO_4 irritant was described in the reports of Bushtueva,[45] Sim and Pattle,[30] and Amdur et al.[49] This is not surprising, since Wilson and La Mer,[50] in 1948, proved that the retention of inhaled aerosol particles decreased as the respiratory rate increased. Bushtueva[45] found clear-cut reflex changes in respiratory rhythm and amplitude during multiple exposures of volunteers to a H_2SO_4 mist of 1.8 to 2.0 mg/m^3. At concentrations of 1.0 to 1.1 mg/m^3, changes in respiration were also noted, though at a decidedly lower rhythm and amplitude. However, she was unable to demonstrate respiratory changes when the mist concentration was below 1.0 mg/m^3, although this may have been due to differences in the degree of "aerosol dispersion."

Thus, as the respiratory rate increases, there is a definite reduction in the percentage of H_2SO_4 mist retained by the respiratory tract. The change in respiratory rhythm and amplitude may very well be thought of as a reflex protective mechanism preventing the retention of the irritant[49,50] and thereby decreasing its toxic effects. By measuring the total volume of air breathed, the concentration of the H_2SO_4 aerosol in the mixing chamber, and its concentration in exhaled air, Amdur[49] was able to measure the percent retention of inhaled H_2SO_4. Average retention varied from 50 to 87 percent when exposure concentrations of 0.4 to 1.0 mg/m^3 were used. There are two reasons for this relatively high retention. First, the aerosol levels used in the experiment increased the respiratory rate by only 35 percent (i.e., by 5 to 7 breaths per minute), certainly not enough to reduce retention much from baseline values, and, second, H_2SO_4 droplets have a strong affinity for moist surfaces such as would be encountered in mucous membranes of the respiratory tract.

It was noted above that that the respiratory rate and pulmonary air-flow resistance in human volunteers rose rapidly as exposure concentrations of H_2SO_4 aerosol were increased. Symptomatically, bronchospasm was also evident in the healthy subjects, presenting a kaleidoscopic picture with the chief manifestations being wheezing, increased secretions, dyspnea, spasmodic coughing, and occasional chest pain. These symptoms have appeared in various combinations and with varying intensity depending upon the aerosol concentration and length of exposure.[51] A chronic bronchitis was even noted by one observer team[30] during long-term intermittent exposure to low levels of H_2SO_4 aerosol.

Bronchospasm, increased upper respiratory tract secretions, and a rapid respiratory rate all contributed to the consistent finding of an elevated pulmonary air-flow resistance in all volunteers exposed to mist levels greater than 0.35 to 0.5 mg/m^3. All subjects used in the previous experiments were young healthy adults who could easily compensate for the increased resistance imposed on their breathing. However, elevated airway resistance severely embarrasses breathing in individuals already burdened by cardiorespiratory difficulties, and further enhances the difficulty of obtaining needed oxygen. Moreover, these effects impair gaseous exchange in the lungs and lead to an increased accumulation of carbon dioxide with its resultant respiratory acidosis. The production of an acidotic condition superimposed on a restricted oxygen intake in pulmonary cripples goes far to explain the effects seen when H_2SO_4 aerosol concentrations rapidly rise above threshold levels.[52]

Sim and Pattle[30] studied the response of healthy males, aged 18 to 46, to sulfuric acid mist. They made 183 exposures of 10 minutes by mask and 316 60-minute chamber exposures to an acid mist at a relative humidity of 62 percent. The droplet size was 1 micrometer and the strength of the sulfuric acid droplets was 10N. They also made a total of 40 exposures in the chamber at 91 percent relative humidity. The droplet size was 1.5 micrometer and the normality was 4N, and concentrations of the dry mist were 3 to 39 mg/m^3 and of the wet mist were 11.5 to 38 mg/m^3. The reporting of the results was vague. The sulfuric acid was more irritant at high humidity, when exposure at 20.8 mg/m^3 for 30 minutes produced intense coughing which did not cease entirely throughout the exposure period. The mist was described as "almost intolerable at the onset" but the men "were able to continue for a period of 30 minutes." No airway resistance measurements could be made during the first 10 minutes. When the coughing had diminished enough to permit measurement, the increases ranged from 43 to 150 percent above normal. When the exposure was to dry mist at 39 mg/m^3 for a 60-minute exposure, the mist was well tolerated and there was minimal coughing. All 12 men in the group showed an increase in resistance with a range of changes from 35.5 to 100 percent above normal. As mentioned previously, the investigators themselves became sensitive to both sulfur dioxide and sulfuric acid mist. One of them had his last exposure to 39.4 mg/m^3 of the dry mist, and he then exhibited chest symptoms for the remainder of the exposure and wheezed persistently for 4 days thereafter. Two subjects exposed to sulfuric acid developed long-lasting bronchitic symptoms.

Two points of value from this study apply to toxicological evaluation. One is the observed effect of high humidity on the irritant potency of sulfuric acid. The other is that, in terms of sulfur equivalent, sulfuric acid is considerably more irritant to human subjects than is sulfur dioxide.

Lawther[53] believes that experiments in the laboratory in which normal subjects have inhaled sulfuric acid mists of various particle sizes but of concentrations of approximately 1 mg/m^3 have failed to produce significant alterations in airway resistance. He mentions that certain individuals show a response to sulfur dioxide at concentrations at which the group tested as a whole did not respond and suggests that no such hypersensitivity to sulfuric acid has been recorded. These opinions are presumably based on the author's own unpublished data and are difficult to evaluate.

C. NASAL ADSORPTION

Frank and Speizer[54,54] made measurements of the uptake and release of sulfur dioxide by the human nose. Subjects breathed through a face mask with special ports for sampling tubes. Samples could be taken within the mask within the nose 1 to 2 centimeters beyond the alae nasi, and within the oropharynx as far back as could be tolerated. The electrical conductivity method was used to determine the concentration of sulfur dioxide in samples taken during both inspiration and expiration. The concentration within the mask averaged about 46 mg/m^3 (16 ppm) and exposures were of 25- to 30-minutes duration. The average concentration in the nose was about 39.5 mg/m^3 (13.8 ppm), representing a decrease of 14 percent. The concentration at the oropharynx was too small to be measured accurately. During exhalation, the sample from the noise contained an average of 6 mg/m^3 (2 ppm), suggesting a desorption from the mucosa during exhalation.

D. EFFECT ON REMOVAL OF MUCUS FROM THE RESPIRATORY TRACT

In a study[56] of the effect of sulfur dioxide on the rate of removal of mucus from the respiratory tract of human subjects, exposures to from about 29 to about 43 mg/m^3 (10 to 15 ppm) for 1 hour produced a 10- to 15-percent decrease in the clearance rate, while a concentration of from about 72 to about 86 mg/m^3 (25 to 30 ppm) caused a 45- to 50-percent decrease and from about 140 to about 160 mg/m^3 (50 to 55 ppm) caused a 65- to 70-percent decrease. It was not reported whether or not the subjects were nose-breathing during exposure.

E. SENSORY THRESHOLD CONCENTRATIONS

The kinds of response to sulfur dioxide discussed in this section, although not strictly within the realm of toxicology, are appended here because the data are closely related to the discussion in this Chapter.

Many recent investigations in Russia have been directed toward determining sulfur oxides threshold concentrations for various sensory responses. These investigations have included determination of odor thresholds and the effects of sulfur dioxide on optical chronaxie, sensitivity of the dark-adapted eye to light, interruption of the alpha (α) rhythm in electroencephalograms, and interference with cortical conditioned reflexes as shown by electroencephalograms. Most of these investigations have been summarized, and the more recent methodology described, by Ryazanov.[57]

1. Odor Perception Threshold

An odor threshold is typically determined in a well-ventilated chamber containing 2 orifices from which emerge 2 small streams of gas, one being very pure air and the other being a stream of the test gas. The subject sits in front of the apparatus, sniffs both orifices, and points out the odorous one. This experiment is repeated with the same concentration of test gas over a period of several days. The experiment is performed with increasingly reduced concentrations until the subject, in the majority of instances, denies the presence of an odor or gives erroneous answers. The threshold concentration for the most sensitive subject in a group of volunteers is defined as the threshold for odor perception.[57]

Using the 2-orifice apparatus described above, Dubrovskaya[58] conducted sulfur dioxide odor perception threshold tests on 12 subjects. Sulfur dioxide concentrations of 0.5 to 13 mg/m^3 (0.17 to 4.6 ppm) were used in 530 threshold determinations. Six test subjects sensed the odor of sulfur dioxide in the range 2.6 to 3.0 mg/m^3; four subjects sensed the odor in the range 1.6 to 2.0 mg/m^3; one sensed the odor in the range 2.1 to 2.5 mg/m^3; and one sensed the odor in the range 3.1 to 3.6 mg/m^3. Thus, the average sulfur dioxide odor threshold concentration was 2.3 to 2.9 mg/m^3 (0.80 to 1.0 ppm), and for the more sensitive of these persons it was 1.6 to 2.0 mg/m^3 (0.56 to 0.71 ppm); it should be noted, however, that most of the subjects were of an age at which odor perception was presumed to be most sensitive.

Bushtueva[45] reported that among 10 test subjects the minimum concentration of sulfuric acid aerosol (particle size not given) which was sensed by odor ranged from 0.6 to 0.85 mg/m^3 (average 0.75 mg/m^3). In tests made on five subjects[59] a combination of sulfur dioxide at 1 mg/m^3 (0.35 ppm) and sulfuric acid mist at 0.5 mg/m^3 was below the odor threshold.

Popov et al.[60] used an apparatus in which the sulfur dioxide concentration could be changed rapidly and showed that the odor of sulfur dioxide could be detected at concentrations of 4 mg/m^3 (1.4 ppm). At 4.0 to 6.5 mg/m^3 (1.4 to 2.3 ppm), the majority of their test subjects perceived the gas as a strong odor; a few perceived it as a faint odor. Subjects described concentrations of sulfur dioxide above 8.5 mg/m^3 (3.0 ppm) as having a very sharp odor. The number of subjects involved in these studies was not stated.

Recent determination of sulfur dioxide odor thresholds[61] conducted for the Manufacuring Chemists' Association gave somewhat lower values than those cited above. The concentrations at which first one-half and then all of the panel members could positively recognize the odor were reported both to be 1.3 mg/m^3 (0.47 ppm). The details of the test procedure are thoroughly discussed in the report, but one important aspect is reiterated as a reminder that odor thresholds usually represent values derived under ideally suited conditions and with trained individuals. The investigators, who were highly qualified to judge on the basis of substantial experience with consumer evaluation of known flavor and odor situations, derived threshold values, in test rooms under ideal conditions, lower than those which would be recognized by the majority of a population under ordinary atmospheric conditions. This does not mean that normal individuals exposed to sulfur dioxide under ideal test conditions could not perceive the 1.3 mg/m^3 (0.47 ppm) level indicated, but because of background odor and lack of awareness or concern with ambient odor conditions, such individuals in an everyday situation would probably be less responsive to this low concentration than are subjects undergoing a test.

2. Sensitivity of the Dark-Adapted Eye

The sensitivity of the eye to light while a subject is in darkness increases with time. Several investigations have been made of the effects of inhalation of sulfur oxides on this sensitivity. Typically, measurements of a subject's normal sensitivity are taken in a dark, well-ventilated chamber in complete silence (sudden stimuli, including noise, may change the sensitivity). Each subject is tested once daily following preliminary conditioning at a high light level. Light sensitivity is measured at 5- or 10-minute intervals, and a normal curve of increasing sensitivity to light is established from measurements taken over a period of 7 to 10 days.[57]

Dubrovskaya[58] studied the effect of inhaling sulfur dioxide in concentrations from 0.96 to 19.2 mg/m^3 for 15 minutes before measuring light sensitivity during dark adaptation. She reported that light sensitivity was increased by sulfur dioxide concentrations of 0.96 to 1.8 mg/m^3 (0.34 to 0.63 ppm), that the increase in sensitivity reached a maximum at concentrations of 3.6 to 4.8 mg/m^3 (1.3 to 1.7 ppm), and that further increases in the sulfur dioxide concentration resulted in progressive lowering of eye sensitivity to light until at 19.2 mg/m^3 the sensitivity was identical with that of the unexposed subject.

In exposures during light adaptation, sulfur dioxide concentrations of 0.6 to 7.2 mg/m^3 (0.21 to 2.5 ppm) caused slight increases in eye sensitivity. Maximum sensitivity was attained at 1.5 mg/m^3 (0.52 ppm); at higher concentrations the increased sensitivity began to abate. Two human subjects were used in these experiments. The odor threshold was between 2.5 and 3.0 mg/m^3 for one subject and between 3.0 and 3.6 mg/m^3 for the other, so that changes in sensitivity to light during dark adaptation were caused by sulfur dioxide concentrations below the odor threshold.

Bushtueva[45] studied the effect of sulfuric acid mist on the sensitivity to light of two test subjects. The test periods were 60, 90, and 120 minutes. During the first half hour, sensitivity was measured every 5 minutes, and after that every 10 minutes. In each subject a control curve was established by 7 repeated tests, and then the effect on light sensitivity of sulfuric acid aerosol exposure for 4 minutes and for 9 minutes at the 15th and 60th minutes, respectively, was determined. With sulfuric acid mist of undetermined particle size at a concentration of 0.6 mg/m^3, a just detectable increase in light sensitivity was found as a result of the exposure at the 15th minute, but no detectable effect was observed as a result of the exposure at the 60th minute. Concentrations in the range of 0.7 to 0.96 mg/m^3 brought about a well-defined increase in light sensitivity. With 2.4 mg/m^3, increased sensitivity to light was elicited by the exposures at both the 15th and 60th minutes of the test; normal sensitivity was restored in 40 to 50 minutes.

Bushtueva[59] studied the effect of sulfur dioxide, sulfuric acid mist, and combinations of the two on sensitivity of the eye to light in 3 subjects. The combination of sulfur dioxide at 0.65 mg/m^3 (0.23 ppm) with sulfuric acid mist at 0.3 mg/m^3 resulted in no change in sensitivity of the eye to light. An increase of approximately 25 percent in light sensitivity resulted from exposure to either sulfur dioxide at about 3 mg/m^3 (1.0 ppm) or sulfuric acid mist at 0.7 mg/m^3. The combination of sulfur dioxide at 3 mg/m^3 with sulfuric acid mist at 0.7 mg/m^3 resulted in an increase of approximately 60 percent in light sensitivity. Exposures lasted for 4-1/2 minutes.

3. Interruption of Alpha Rhythm

The electroencephalogram is a composite record of the electrical activity of the brain recorded as the difference in electrical potential between 2 points on the head. In the adult, the electroencephalogram characteristically shows a fairly uniform frequency from 8 to 12 cycles per second in the posterior head regions. Variations occur with age, and the state of wakefulness and attentiveness, or as a result of incoming sensory stimuli from exteroceptive or interoceptive receptors. The dominant frequency is inhibited or attenuated by eye opening and by mental activity.[62]

Subjects with well-defined α-rhythms studied in a silent and electrically-shielded chamber show a temporary attenuation of the α-rhythm each time they are given a light signal. When the light is excluded, the α-rhythm returns to normal. A concentration of test gas is determined which is so low that by itself it does not cause attenuation of the α-rhythm. A subject breathes the gas at this concentration, and then he receives the light signal. After exposure to this sequence (gas then light) several times (5 to 30 times in 1 day), a subject will show attenuation before he receives the light signal; that is, he responds to the unperceived odor. The unperceived odor thus becomes the conditioning stimulus and brings about the so-called conditioned electrocortical reflex.[57]

Bushtueva et al.[63] reported that 20-second exposures of 6 human subjects to sulfur dioxide concentrations from 0.9 to 3 mg/m^3 (about 0.3 to about 1.0 ppm) produced attenuation of the α-wave lasting 2 to 6 seconds; at concentrations of 3.0 to 5.0 mg/m^3 (about 1.0 to 1.7 ppm) attenuation lasted throughout the 20-second exposure. Exposures to 0.6 mg/m^3 (about 0.2 ppm) did not cause attenuation of the α-wave. Exposures to sulfuric acid mist at 0.6 to 0.75 mg/m^3 caused attenuation of the α-wave, whereas exposures to 0.4 to 0.5 mg/m^3 did not. For both substances, the threshold for attenuation of the α-wave is the same as the odor threshold or the threshold of irritation of the respiratory tract. In other experiments, Bushtueva demonstrated that electrocortical conditioned reflexes could be developed with sulfur dioxide at 0.6 mg/m^3 (about 0.2 ppm) or with sulfuric acid mist at 0.4 mg/m^3, but not with lesser concentrations of either substance. Finally, Bushtueva[64] demonstrated that combinations of sulfur dioxide at 0.50 mg/m^3 (0.17 ppm) with sulfuric acid mist at 0.15 mg/m^3 or sulfur dioxide at 0.25 mg/m^3 (0.087 ppm) with sulfuric acid mist at 0.30 mg/m^3 could produce electrocortical conditioned reflexes.

4. Optical Chronaxie

Chronaxie is defined as the time required for excitation of a nervous element by a definite stimulus. In the determination of optical chronaxie, a weak electrical current is applied to the eyeball to give the sensation of a light flash. For each subject there is an intensity of stimulation (measured in volts) below which no sensation of light takes place. The time required for this minimal voltage to produce the sensation of light in a subject is the optical chronaxie for the subject. According to Pavlovian theory, the excitation of one area of the cerebral cortex may inhibit the excitation of other areas through the rule of induction.[57] It has therefore been postulated that excitation of the olfactory sensory area by the oxides of sulfur inhibits the light-sensing area of the cerebral cortex and thus increases optical chronaxie.

Bushtueva[59] studied the effects of different concentrations of sulfur dioxide, sulfuric acid mist, and combinations of the two on the optical chronaxie of three subjects. Optical chronaxie was determined in each test subject at 3-minute intervals as follows: at the start and on the 3rd, 6th, 9th, 12th, and 15th minutes. Between the 6th and 9th minutes the subjects inhaled sulfur dioxide, sulfuric acid mist, or their combination for 2 minutes. In each subject the threshold concentrations of sulfur dioxide and sulfuric acid mist were first determined independently, and then threshold concentrations for combinations of the two were determined.

Results presented for one subject were:

a. Neither sulfur dioxide at 900 $\mu g/m^3$ nor sulfuric acid mist at 600 $\mu g/m^3$ produced increased optical chronaxie, but the combination of these concentrations produced a 16 percent increase in optical chronaxie;

b. Concentrations of sulfur dioxide at 1200 μg/m^3 with sulfuric acid mist at 400 μg/m^3 produced no increase in optical chronaxie; and

c. Concentrations of either sulfur dioxide at 1500 μg/m^3 or sulfuric acid mist at 750 μg/m^3 increased optical chronaxie, and the effects of the combination at these concentrations were additive. Similar results were reported for the other subjects.

The data obtained by Bushtueva[64] are summarized in Table 6-1. Consideration of the levels noted provides information which may be relevant to the establishment of "Level I" and "Level II" of the World Health Organization's "guides to air quality."[65] These "guides," equivalent in usage to our term "criteria," cover sets of concentrations and exposure times at which specified types of effects are noted or at

Table 6-1. THRESHOLD CONCENTRATIONS OF SULFUR DIOXIDE, SULFURIC ACID, AND THEIR COMBINATIONS FOR VARIOUS RESPONSES[64]

Procedure Used	Threshold Concentration			
	H_2SO_4	SO_2	H_2SO_4 +	SO_2
	μg/m^3	μg/m^3	μg/m^3	μg/m^3
Threshold Concentration of Irritation Effects and Odor Perception	600–850	1600–2600	>300	500
Data Obtained by the Method of Eye Adaptation to Darkness	630–730	920	>300	500
Data Obtained by the Method of Optical Chronaxie	730	1500	600	1200
Encephalographic Method	630	900	>300	500
"Electrocortical" Conditioned Reflex	400	600	150 300	500 250

which no effect is noted. The definitions of these levels are as follows:

Level I (Range I) Concentrations and exposure times at or below which, according to present knowledge, neither direct nor indirect effects (including alteration of reflexes or of adaptive or protective reactions) have been observed.

Level II (Range II) Concentrations and exposure times at and above which there is likely to be irritation of the sensory organs, harmful effects on vegetation, visibility reductions, or other adverse effects on the environment.

Level III (Range III) Concentrations and exposure times at and above which there is likely to be impairment of vital physiological functions or changes that may lead to chronic diseases or shortening of life.

Level IV (Range IV) Concentrations and exposure times at and above which there is likely to be acute illness or death in susceptible groups of the population.

The practical ramifications of these neurophysiological responses have not been explored. In addition, one should be cautioned in the interpretation of these data since there have been no replicate studies to confirm the reported neurophysiological responses and information concerning the experimental conditions was less than adequate.

F. DERMATOLOGIC EXPOSURE

Sulfur is used for desensitization in various allergic states and is applied topically usually in an ointment. Because of this use sulfur and the sulphides are generally held to never cause allergy. It appears, however, that certain persons can be sensitized to sulfur and its compounds. At least one case of skin allergy attributed to gaseous SO_2 is reported in the literature. Pirila[66] reports a case of a male worker 30-years of age in a sulphite cellulose factory with no previous history of allergic response who developed itching, red patches, and wheals with white borders on his palms and other areas of the skin. The lesions disappeared almost totally when he was away from work for several days. He worked near a reservoir into which hot waste liquor from the sulphite spirit mill was taken every three hours, thus exposing him to gaseous SO_2. He remained well so long as he was away from work. On returning to work, he developed wheals the first evening. For six days he avoided the gas as much as possible and, when exposed, used a gas mask. He had no eruptions. Three other trials without the gas mask resulted in recurrence. In clinical trials the patient was exposed to 107.5 mg/m^3 (39.8 ppm) SO_2 in a room for one hour and developed urticarial wheals on the trunk and extremities in seven hours. It grew worse for the next nine hours and then gradually disappeared. The author considers this to be positive clinical identification of a case of urticaria caused by exposure to SO_2. Thus, in certain sensitive persons, air pollution, especially in industrial exposure, should be considered as an etiologic factor in skin disease.

G. SUMMARY

Various animal species, including man, respond to sulfur dioxide by bronchoconstriction, which may be assessed in terms of a slight increase in airway resistance. Normal individuals, exposed to sulfur dioxide via the mouth, exhibit small changes in airway resistance which are often insufficient to produce any respiratory symptoms. The effects may be even smaller when the subject breathes through his nose.

Laboratory observations of respiratory irritations suggest that most individuals will show a response to sulfur dioxide at concentrations of about 14 mg/m^3 (5 ppm) and above. At concentrations of about 3 to about 6 mg/m^3 (1 to 2 ppm), an effect can be detected only in certain sensitive individuals, and on occasion, exposures to about 14 to about 30 mg/m^3 (5 to 10 ppm) have been shown to cause severe bronchospasm in such persons; no further special study at lower concentrations has been carried out with these individuals. The exposure of the more sensitive individuals to about 3 mg/m^3 (1 ppm), although it does not produce severe bronchospasm, does elicit a detectable response.

Sulfuric acid is a much more potent irritant to man than is sulfur dioxide, and its effects are highly dependent on particle size. Insufficient data are available for quantitative assessment of the health hazard. There is inadequate information on the response of human subjects to any of the other particulate sulfates. Nasal absorption and desorption of oxides of sulfur, and the effect of the oxides on the removal of mucus from the respiratory tract are briefly considered.

In most of the studies discussed, an increase in pulmonary flow resistance was the indicator of response employed. However, the concentrations of oxides of sulfur just needed to elicit certain sensory responses are presented, although the practical ramifications of these neurophysiological responses have not been fully explored. These values may ultimately have significance for the establishment of Levels I and II of air quality as promulgated by the World Health Organization.

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Chapter 7

COMBINED EFFECTS OF EXPERIMENTAL EXPOSURES TO SULFUR OXIDES AND PARTICULATE MATTER ON MAN AND ANIMALS

A. INTRODUCTION

The problem of interactions of irritant gases and particulate material is one of greatest interest in air pollution toxicology. Its implications are far broader than the present specific discussion of the effect of particulate material on the response to sulfur dioxide. For a treatment of the broader aspects of the problem, see Chapters 9 and 10 in the companion document, Air Quality Criteria for Particulate Matter.

B. EVALUATION BY MORTALITY AND PATHOLOGY IN ANIMALS

1. Sulfur Dioxide, Sulfuric Acid, and Particles

Schnurer[1] exposed rabbits and rats (23 hours per day for 80 days) and mice (17 days) to atmospheres produced from burning equal amounts of anthracite coal, coke, and bituminous coal. The resulting sulfur dioxide concentrations were 5.46 mg/m^3 (1.91 ppm) for anthracite coal, 26.1 mg/m^3 (9.12 ppm) for coke, and 21.5 mg/m^3 (7.51 ppm) for bituminous coal. The corresponding particle concentrations were 312, 370, and 4,410 particles per cubic centimeter. The control atmosphere contained 125 particles per cubic centimeter. Taking the weight gain of control animals as 100 percent, the rats exposed to anthracite smoke gained 105 percent, the rats exposed to coke smoke gained 114 percent, and the rats exposed to bituminous coal smoke gained 75 percent. With the rabbits these values were 84 percent, 77 percent, and 9 percent respectively. The hemaglobin percentage and the red and white blood cell counts rose in all groups, but this rise was less pronounced in the rabbits exposed to anthracite smoke. The greatest changes in the above measurements, the greatest number of uncomplicated pneumonias, and the greatest incidence of bronchitis were observed in the animals exposed to bituminous coal smoke. No significant pathological change could be detected in the lungs of animals exposed to coke or anthracite smoke 2-1/2 months or 14 months after exposure. Animals exposed to bituminous coal smoke developed evidence of fibrosis, proliferation of the bronchial epithelium, and marked peribronchial lymphoid hyperplasia.

The exposures to anthracite coal smoke and coke smoke were essentially equivalent in terms of particle concentration, but the smoke from the coke contained about 26/mg/m^3 (9 ppm) sulfur dioxide as opposed to about 6 mg/m^3 (2 ppm) for the anthracite coal smoke. Neither of these exposures produced pathological alterations in the lungs. The smoke from coke and bituminous coal contained about 26 mg/m^3 and about 23 mg/m^3 (8 ppm) sulfur dioxide respectively, but the particle concentratior of the bituminous coal smoke was over 10 times that of the smoke from the coke. The bituminous smoke produced pathological alterations which were not observed in animals exposed to the smoke from the coke. The pathological alterations observed in the animals exposed to bituminous coal smoke may possibly be associated with the simultaneous presence of high levels of sulfur dioxide and smoke. Unfortunately, however, the experiments do not allow a simple interpretation.

Susceptibility to infection by pneumococci of rats exposed to coal dust or smoke has been studied.[2] Sulfur dioxide concentrations in the coal smoke ranged between 2 and 4.6 mg/m^3 (.7 and 1.6 ppm) and smoke concentrations would have been considered as "dense" on visual inspection (equivalent to about a No. 3 reading-on the Ringelmann Chart.)

Exposures ranged from 2 to 154 days, and no difference was noted between the control animals and exposed animals in regard to mortality or susceptibility to infection. On the other hand, the strain of rats used normally are known to develop areas in the lung which are filled with mucus or pus, and the incidence of this condition was 20 percent in the control animals and 40 percent in animals exposed to smoke for more than 20 weeks.

Pattle and Burgess[3] studied the effect of mixtures of sulfur dioxide and smoke on mice and guinea pigs. The concentrations of sulfur dioxide used were in the range of 2,700 to 12,000 mg/m^3 (940 to 4,200 ppm) and the smoke concentrations were in the range of 50 to 135 mg/m^3. The end point was the dosage required to produce death. With concentrations of this magnitude, the results obtained have little applicability to air pollution criteria. Although they found that the lethality of mixtures of sulfur dioxide and smoke was greater than the lethality of the sulfur dioxide alone, they considered the effect to be a simple additive one resulting from the action of smoke in blocking the bronchi and alveoli.

Salem and Cullumbine[4] studied the effects of kerosene smoke on the acute toxicity to guinea pigs and mice of various irritants, among them sulfur dioxide and sulfuric acid. As in the work of Pattle and Burgess,[3] the concentrations were orders of magnitude greater than those found in polluted atmospheres. Sulfur dioxide concentrations were between 3,400 and 7,700 mg/m^3 (1,200 and 2,700 ppm) while sulfuric acid concentrations were in the range 55 to 174 $\mu g/m^3$. The smoke concentrations were presumably about 600 mg/m^3, although it is not clearly stated whether this was the concentration used in the combinations. The end point was the mean fatal dose. The administration of smoke prior to exposure to the irritant substances did not alter the toxicity in contrast with a report by Pattle and Burgess[3] of a protective effect. The effect of smoke on the toxicity of the various irritants was highly variable when the two agents were given simultaneously. In guinea pigs the toxicity of sulfur dioxide was decreased by the smoke and in mice it was increased; the toxicity of sulfuric acid was increased by the smoke.

Gross et al.[5] reported the typical lesions of pneumonitis in the lungs of hamsters, rats, and guinea pigs exposed to "a sufficiently large number of carbon particles with either adsorbed sulfur dioxide or nitrogen dioxide." Exposure was 8 hours per day, 5 days a week, for 4 weeks. The histological sections from animals sacrificed about a month after the end of exposure, indicated that the lesions were persistent. The lesions were concentrated in the regions of the respiratory bronchioles and alveolar ducts and consisted of cellular wall thickening. Data were not provided about the amount of irritant absorbed by the activated carbon particles, or the particle size of the carbon, nor on the meaning of "a sufficiently large number of carbon particles." It was concluded that under certain experimental conditions the irritant gases were capable of rendering normally inert particles irritant, but these conditions were not defined.

2. Sulfur Dioxide and Sulfuric Acid

The effect of a combination of sulfur dioxide and sulfuric acid on guinea pigs has been reported.[6] Only one combination of concentrations was used, 255 mg/m^3 (89 ppm) sulfur dioxide and 8 mg/m^3 sulfuric acid (1-micrometer MMD). Eight animals were exposed to this combination for

8 hours and 2 of these animals were reexposed 4 days later to the same combination. Since only one combination of concentrations was used in these experiments, they do not provide evidence for synergism, and the author concludes that further studies are needed before the results can be interpreted.

Bushtueva[7,8] reported that exposure of guinea pigs to 0.5 mg/m^3 sulfuric acid produced only slight lung irritation. When the sulfuric acid was combined with about 0.9 mg/m^3 (0.3 ppm) sulfur dioxide, considerable changes in lung pathology were observed 2 months after a 2-week exposure. These changes included thickening of the interalveolar septa, formulation of lympathic folliculi, and perivascular and peribronchiolar fibrosis. Histamine content of the lungs increased concomitantly with the pathology. It is difficult to draw any unified conclusions of practical value from these experiments, since none was designed so that the joint toxic action could be satisfactorily assessed.

In a later paper, Bushtueva[9] examined the effects on white mice of SO_2 and H_2SO_4 aerosol administered separately and combined. In the mixed atmosphere concentration SO_2 was 4.79 mg/m^3 and H_2SO_4 was 0.92 mg/m^3. There was little effect on general external indices such as behavior, condition, weight, etc. The simultaneous combined action of $SO_2 + H_2SO_4$ produced a more profound chronaxy distortion, hastened the rate of acetylcholinechloride decomposition (reflecting a rise in cholinesterase activity), no significant changes in the effect of total blood serum protein, and no significant change in elimination of coproporhyrin. Overall, the author concluded that the prolonged interrupted inhalation of air containing a mixture of SO_2 and H_2SO_4 affected the mice in a synergistic (additive) manner.

C. EVALUATION BY PULMONARY FUNCTION IN ANIMALS

The increase in pulmonary flow resistance has been used by Amdur and her coworkers[10-12] to study the effect of simultaneous exposure of guinea pigs to irritant gas and to an aerosol. Three experiments deal with the situation in which both the gas and the aerosol are irritant. Two of these use sulfur dioxide and sulfuric acid mist,[11] and one uses sulfur dioxide and zinc ammonium sulfate.[12]

In the sulfur dioxide-sulfuric acid experiments the concentrations employed were high (about 270 mg/m^3 (100 ppm) sulfur dioxide and 8 to 15mg/m^3 sulfuric acid). When the sulfuric acid had a particle size of 0.8-micrometer MMD, the joint toxic action was synergistic. When the acid particles were larger, with an MMD of 2.5-micrometers, the response to the mixture was slightly less than the response to the higher level of sulfur dioxide alone.

The concentrations used in the experiment with zinc ammonium sulfate and sulfur dioxide were at about the concentrations at which these substances were estimated to have been present during the Donora episode. Zinc ammonium sulfate, 0.29-micrometer MMD, was used at 0.25 mg/m^3, and the sulfur dioxide was at about 6 mg/m^3 (2 ppm). The effect of the combination demonstrated synergism as had been observed with the smaller-sized sulfuric acid. An explanation for these results may go beyond the simple hypothesis that adsorption of sulfur dioxide by the smaller-size acid particles, which penetrated the deeper areas of the lung, increased the amount of sulfur dioxide reaching the alveoli.

Other experiments have studied the combined effects of sulfur dioxide and "inert" aerosols (in the sense that they do not produce a statistically significant alteration in the flow-resistance of guinea pigs exposed for the standard 1-hour test period of this work).[11] The initial "inert" aerosol used as a standard was sodium chloride at a concentration of about 10 mg/m^3 in combination with a variety of irritant gases. This concentration of sodium chloride as an aerosol of 2.5-micrometer MMD did not alter the response to sulfur dioxide. In all subsequent experiments a 1-percent sodium chloride solution was dispersed as an aerosol with a count mean size of about 0.04-micrometer (σg=3.3). This aerosol did potentiate the response to the sulfur dioxide when tested over the concentration range of about 6 to 570 mg/m^3 (2 to 200 ppm).[11] The data were were examined by comparing the concentration of gas alone required to produce the same percentage increase in resistance. Over the concentration range of 72 to 715 mg/m^3 (25 to 250 ppm), a given concentration of sulfur dioxide plus-aerosol produced about the same response as was produced by 2.5 to 3 times that concentration of the gas alone.

At lower concentrations the relationship changed, and at 6 mg/m^3 (2 ppm) the gas plus aerosol produced the same response as 30 times that concentration of gas alone. A comparison of the dose-response curves for sulfur dioxide and sulfuric acid (0.8-micrometer) gave a similar picture.

At the higher concentration ranges, the response to sulfuric acid was uniformly 15 to 20 times the response to an equivalent concentration of sulfur dioxide, but at 1.4 mg/m^3 (0.5 ppm) sulfuric acid the response is equivalent to the response to 170 mg/m^3 (60 ppm) sulfur dioxide rather than to 23 to 29 mg/m^3 (8 to 10 ppm) as would have been predicted. However, for the entire concentration range tested, response to sulfuric acid was about 3 times the response to an equivalent amount of sulfur dioxide in the presence of the aerosol, which suggested that the gas-aerosol mixture had the same biological effect as sulfuric acid. The implication is that the sulfur dioxide had become attached to the particles in some manner and created an irritant aerosol.

Decreasing the concentration of the sodium chloride aerosol to about 4 mg/m^3 decreased the potentiating effect.[13] The dose-response curve is parallel to that obtained with the higher concentration, but only one point, that at 57 mg/m^3 (20 ppm), is greater than the corresponding point for sulfur dioxide alone. This decrease in potentiating effect with decreased aerosol concentration again suggested that the response was mediated through the formation of an irritant aerosol. It also suggested that the irritant aerosol formed by sodium chloride with sulfur dioxide was not a very potent irritant, since the effects had essentially vanished at an aerosol level of 4 mg/m^3.

Another factor suggesting the formation of an irritant aerosol comes from examination of the postexposure data. After exposures to gas-aerosol combinations were terminated, the resistance values remained above control values rather than returning to the preexposure level within an hour as had occurred after exposure to these levels of irritant gas alone.[14] As was pointed out at the end of Section C of Chapter 5, the return to control values was much slower when the irritant had been particulate matter than when it had been gaseous. The response to 323 mg/m^3 (113 ppm) sulfur dioxide alone and to 74 mg/m^3 (26 ppm) sulfur dioxide plus 10 mg/m^3 of NaCl aerosol was similar during the 1-hour exposure period. The animals exposed to the higher level of sulfur dioxide alone had shown a complete return to preexposure resistance values by 45 minutes after the exposure ended. Those exposed to the lower concentration plus aerosol still showed elevated resistance values 2 hours after the end of the exposure.

There is also evidence that the level of elevated resistance during the postexposure period is related to the concentration of the particulate material present. First of all, the time course of the response to various sulfur dioxide concentrations in the presence of a fixed sodium chloride aerosol concentration (10 mg/m^3) was examined. At the end of the exposure period the resistance values were higher at higher sulfur dioxide concentrations. One hour after the exposure ended they were all above control values but were all of the same order of magnitude, regardless of sulfur dioxide concentration. Two hours after the end of the exposure, the resistance values of the animals exposed to sulfur dioxide concentrations of 72 mg/m^3 (25 ppm) or above had increased slightly. The animals exposed to about 6 mg/m^3 (2 ppm) had returned to preexposure levels by 2 hours after the end of exposure.

Next, the total amount of aerosol was reduced in 2 ways: by reducing the concentration to 4 mg/m^3 for 1 hour, and by exposing animals for only half an hour to a 10 mg/m^3 concentration.[10] The sulfur dioxide concentration was fixed at about 60 mg/m^3 (20 ppm). The results were entirely consistent with the hypothesis that there was a residual effect from an irritant aerosol which had been formed. An increase in resistance was observed between the first and second postexposure hours when the exposure had been for half an hour, and the resistance continued at about this level for the 5-hour postexposure observation period.

It has also been found that the potentiation of the response to sulfur dioxide by aerosols of sodium chloride is slow to develop.[10,13] When the response to gas alone, and to gas plus aerosol, are compared at 10 minutes there is no apparent difference. In this aspect the response is different from that produced by formaldehyde with sodium chloride[13] or that produced by aerosols of soluble metal salts known to catalyze the oxidation of sulfur dioxide to sulfuric acid.[10]

The solubility of sulfur dioxide in a liquid droplet appears to play some role in its potentiation by inert aerosols. This has been suggested[10] by the way in which the potentiating ability of aerosols of sodium chloride, potassium chloride, and ammonium thiocyanate is related to the solubility of sulfur dioxide in solutions of these salts. At the humidities prevailing in the exposure chamber, these substances would have been present as solid particles which, upon entering the moist respiratory tract, would take up water and become droplets.

Most solid aerosols tested[1] have not potentiated the response to sulfur dioxide, which suggests a role of solubility in potentiation. Thus, spectrographic carbon, activated coconut charcoal, iron oxide fume, triphenylphosphate, fly ash, and manganese dioxide at levels of 8 mg/m^3 or above, produced no detectable effect on the resistance nor did they potentiate the response to levels of sulfur dioxide ranging between approximately 3 and 290 mg/m^3 (1 and 100 ppm). In several of the 19 groups of animals exposed to sulfur dioxide plus solid aerosols, the response was apparently less than that observed with a corresponding concentration of sulfur dioxide alone. The attenuations were not statistically significant for either group of animals exposed to what was termed only "fly ash from an oil-fired burner," one exposure being about 30 mg/m^3 (10 ppm) and another being at about 60 mg/m^3 (20 ppm) sulfur dioxide. When the response data from the two individual experiments were compared with those from response to 60 mg/m^3 sulfur dioxide alone, the attenuating effect was statistically significant. It is also mentioned that while triphenylphosphate aerosols of 0.3-micrometer or 1-micrometer failed to alter the response to sulfur dioxide even when present in concentrations of 50 mg/m^3, aerosols of 2 micrometers had a striking attenuating effect when given with sulfur dioxide, and they also protected against the gas when given prior to exposure to sulfur dioxide.

In another experiment Amdur and Underhill[15] examined the response of guinea pigs to iron oxide fume (Fe_2O_3) and redispersed open-hearth dust. Neither produced detectable respiratory response in the concentration ranges 0.16 ± 0.09 and 7.0 ± 1.6 mg/m^3 for open-hearth dust and 11.7 ± 1.4 and 21 ± 3.2 mg/m^3 for Fe_2O_3. Then animals were exposed to a combination of Fe_2O_3 and SO_2 ranging from 1.0 to 24.0 mg/m^3 Fe_2O_3 and from 4 to 70 mg/m^3 (1.5 to 26 ppm) SO_2. Next, animals were exposed to a combination of open-hearth dust and SO_2 ranging from 0.12 to 0.72 mg/m^3 open-hearth dust and 0.45 to 2.2 mg/m^3 (0.16 to 0.80 ppm) SO_2. Conclusions were that neither iron oxide no open-hearth dust affected the response to SO_2.

The aerosols which appeared to have importance in the potentiation of sulfur dioxide were the aerosols of soluble salts which might catalyze the oxidation to sulfuric acid.[10] Aerosols of ferrous iron, manganese, or vanadium, when used at concentrations of 0.7 to 1 mg/m^3 produced a potentiation of the response. A sulfur dioxide concentration of about 0.6 mg/m^3 (0.2 ppm) produced a resistance increase of about 10 percent when given alone and an increase of about 35 percent when given in the presence of these aerosols. The potentiation was already observable at 10 minutes. It could be demonstrated by qualitative tests for sulfate that there was sulfate present on the aerosol collected from the chamber, which was not the case with sodium chloride aerosols.

These experiments suggest that the nature of the particulate material, as well as its size range are key factors. The aerosols of importance are those capable of dissolving sulfur dioxide and possibly of oxidizing it to sulfuric acid mist.

D. EVALUATION BY PULMONARY FUNCTION IN MAN

Frank et al.[16] examined the response of human subjects to levels of sulfur dioxide of about 3 mg/m^3 (1 ppm), about 15 mg/m^3 (5 ppm), and about 43 mg/m^3 (15 ppm), with and without the addition of sodium chloride aerosol. In the initial experiments, the agents were administered for 10-minute periods in sequence with a 15 to 20 minute recovery period between exposures. In a second series, the gas and gas plus aerosol exposures of each subject were made at least a month apart and were extended to 30 minutes. In the experiments in which the gas and the gas plus aerosol were given in sequence, the response to the second exposure was consistently lower than the response to the first exposure, no matter in which order the gas alone and gas plus aerosol were given. In the second series, when the exposures were a month or more apart, no difference was detected between the response to the gas alone and the response to the gas plus aerosol.

When the data for the control values and the resistance response for the same individual to the same level of sulfur dioxide on different occasions are examined, it is seen that a very dramatic potentiation would have been needed to yield positive results in this study. On one subject studied on seven occasions, the control resistance values ranged from 0.65 to 1.48 cm H_2O/l-sec, a difference of about 128 percent.

The alterations produced by exposure on 3 different occasions to $42\ mg/m^3$ (15 ppm) sulfur dioxide were 86 percent, 58 percent, and 156 percent increases in resistance. Two exposures to $42\ mg/m^3$ sulfur dioxide plus aerosol produced on one occasion an increase of 220 percent and on the other occasion an increase of 42 percent. During three exposures to $42\ mg/m^3$ SO_2, one subject showed the most extreme variation in control resistance (1.13 to 1.46 $cm H_2O/l$-sec. with corresponding resistance increases of 130, 93, and 410 percent). The differences in response on the various occasions were not related to absolute level of control resistance, to functional residual capacity, to time of year, or to the previous total number of exposures. The variations on exposures to gas alone on different occasions were as great as the differences between the response to gas alone and to gas plus aerosol. The study makes apparent the difficulties of studies on human beings.

The potentiating effects on guinea pigs are observed by establishing dose-response curves for a large sample of animals: such studies with human beings are virtually impossible. The study of Frank et al.[16] does, however, present two important conclusions. The first is the demonstration of variability of response to sulfur dioxide on different occasions. The second relates to the data on control resistance values for the same individual on different occasions. The comparison of this variation with the magnitude of change produced by sulfur dioxide exposures serves to set the latter in proper physiological perspective.

Toyama[17] studied the flow resistance response of 13 subjects to sulfur dioxide with and without sodium chloride aerosol. Control measurements were made, and the subjects were then exposed in sequence for 5 minutes to sodium chloride, sulfur dioxide alone, and sulfur dioxide plus sodium chloride. The sulfur dioxide concentrations ranged from 4.6 to 160 mg/m^3 (1.6 to 56 ppm). The sodium chloride aerosol produced no change in resistance. The sulfur dioxide produced an increase in resistance and the sulfur dioxide plus sodium chloride produced a greater increase than the gas alone in all subject. Dose-response curves were plotted for the gas alone and for the gas plus aerosol. There was striking overall resemblance to the dose-response curves for the guinea pig experiments of Amdur.[11]

A comparison of equal response concentrations of gas alone and of gas plus aerosol shows similarity to the animal data in that the ratio is greater at the lower concentrations. The sodium chloride used in these studies had a CMD of 0.22-micrometer. Nakamura[18] studied in a similar manner the effect of sodium chloride with a CMD of 0.95-micrometer on the response of 10 subjects of sulfur dioxide. Again, in every case the response was greater when the sodium chloride aerosol was combined with the sulfur dioxide.

It is tempting to conclude that these studies[17,18] have demonstrated that the human subjects had behaved as did Amdur's guinea pigs. However, this conclusion is not necessarily valid. The exposures of human subjects were for 5 minutes, and it has been indicated[12,13] that in the guinea pig the potentiating effect of sodium chloride on sulfur dioxide is not apparent at 10 minutes. If the two species had been behaving in the same manner, a potentiation would not have been observed in these experiments.

When the exposures were given in sequence, the response to the second exposure (always the combination exposure) was invariably greater than the response to the first exposure. The results of sequential exposures to gas and to gas plus aerosol could be interpreted if data were given for a similar number of subjects exposed twice in this manner to the gas alone. In the 10-minute exposures reported by Frank et al.[16], the sequence of gas and of mixture was varied, but the response to the second exposure was less than the response to the first. As stated earlier, sequential exposures in experiments of this type are understandable as a practical procedure, but they constitute a "toxicological trap" for the unwary which unfortunately is not evaded merely by randomizing the sequence.

Burton et al.[19] found that the presence of 2 to 2.7 mg/m^3 of sodium chloride aerosol below 1-micrometer did not affect the response of 10 subjects to from about 3 to about 9 mg/m^3 (1 to 3 ppm) sulfur dioxide. There was no evidence of alteration of pulmonary mechanics immediately following exposures to this gas concentration, either with or without the added aerosol. This lack of response would have been predicted on the basis of animal experiments with 4 mg/m^3 sodium chloride.[13]

Toyama and Nakamura[20] examined the effect of aerosols of hydrogen peroxide with CMD values of 4.6 and 1.8-micrometers on the response to sulfur dioxide. They give CMD values of 4.6 and 1.8-micrometers for the aerosols, measured in a manner which does not necessarily relate to the airborne size. The hydrogen peroxide concentrations were of the order of 0.3 mg/m^3. Sulfur dioxide concentrations ranged from 4.3 to 170 mg/m^3 (1.5 to 60 ppm). The sulfuric acid concentrations produced by the oxidation of sulfur dioxide were 0.8 to 1.4 mg/m^3 for the larger aerosol and 0.01 to 0.1 mg/m^3 for the smaller aerosol, but the reasons for the differences in acid concentration are not discussed.

The response to the mixture was greater than the response to sulfur dioxide alone. The response was greater with the larger aerosol than with the smaller aerosol and is in accord with the particle-size effect discussed earlier. It is likely that it is also related to the concentration of sulfuric acid formed, since this was reported to be at least 10 times greater when the larger aerosol was used. When the sulfur dioxide exposures were grouped at 3 to 28 mg/m^3 (1 to 10 ppm), 28 to 84 mg/m^3 (10 to 30 ppm), and 84 to 168 mg/m^3 (30 to 60 ppm), the response was graded with concentration in the presence of the smaller aerosol (lower acid concentration) but was uniformly about the same, an increase of 35 to 40 percent in resistance, for the 3 levels of gas when the larger particles (higher acid concentration) were present. These experiments present the same problem of sequential exposures discussed above and do not demonstrate synergism.

The data on the effect of particulate material on the response of human subjects does not consistently demonstrate a potentiation by sodium chloride aerosol or a synergism with sulfuric acid mist. There is some suggestion of such effects in three papers, but lack of adequate control data on repeated exposure to sulfur dioxide alone precludes proper interpretation of these data.

E. SUMMARY

The experiments reviewed use changes in pulmonary function, changes in pathology, and mortality to evaluate possible potentiating or synergistic effects of particulate matter on the toxicity of sulfur dioxide. Only changes in pulmonary function may be studied in experiments on man. Synergism by both irritant and "inert" particles is considered.

Sulfur dioxide in the atmosphere may be partly converted into the more irritant sulfuric acid, especially at high humidity and in the presence of particulate material. The irritant potency of sulfuric acid aerosol in itself is dependent on size and relative humidity.

The potentiation by particulate matter of toxic responses to sulfur dioxide (synergism) has been observed under conditions which would promote the conversion of sulfur dioxide to sulfuric acid. The degree of potentiation is related to the concentration of particulate matter. A threefold to fourfold potentiation of the irritant response to sulfur dioxide is observed in the presence of particulate matter capable of oxidizing sulfur dioxide to sulfuric acid. Aerosols of soluble salts of ferrous iron, manganese, and vanadium have been observed to produce this potentiation, although the concentrations used (0.7 to 1.0 mg/m^3) were considerably greater than any reported levels of the metals in urban air.

Experiments with normal human subjects have failed to demonstrate any consistent potentiation of response to sulfur dioxide by sodium chloride particles. In the guinea pig, sodium chloride is the least effective of the various soluble aerosols that produce any potentiation.

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Chapter 8

EPIDEMIOLOGICAL APPRAISAL OF SULFUR OXIDES

A. INTRODUCTION

Health effects produced by atmospheric sulfur oxides are discussed in this Chapter in terms of epidemiologic studies. Because sulfur oxides tend to occur in the same kinds of polluted atmosphere as particulate matter, few epidemiologic studies have been able adequately to differentiate the effects of the two pollutants. It follows, therefore, that the studies presented in this chapter are frequently identical with those described in the companion document, Air Quality Criteria for Particulate Matter.

Epidemiologic studies, as distinguished from toxicologic or experimental studies, analyze the effects of pollution from ambient exposure on groups of people living in a community. Such studies have the advantage of examining illness where it occurs naturally, rather than in a laboratory, but carry the disadvantage of not being able to control precisely all the factors of possible importance. Nevertheless, the preparation of air quality criteria must rest on epidemiologic studies because of the very severe limitations of toxicologic and industrial studies for this purpose. Other countries, notably the Netherlands and Sweden, have based their air quality criteria solely on epidemiologic studies.

In determining whether or not an association is causal, consideration must be given to several aspects of association which include strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, and analogy.[1] A judgment of the value of an epidemiologic study requires an understanding of these aspects.

Many types of epidemiologic evidence suggest that air pollution may exert considerable influence on the health, as well as on the "satisfaction with life," of major segments of the world population.

Several health indices are described in Section B-1; certain precautions which should be observed in the application of epidemiologic methods to air quality criteria are suggested in Section B-2. The studies themselves are listed in Section C, according to the index employed. Several industrial exposures to the oxides of sulfur are mentioned in Section D, discussing their relevance to the epidemiologic studies.

B. APPLICATION OF EPIDEMIOLOGY TO AIR POLLUTION STUDIES

1. Indices

Various indices of health may be used for correlation with air pollution by the oxides of sulfur. Among the possible indices are:

a. Mortality (greater than expected):

   (1) Deaths from all causes

   (2) Deaths from specific causes

   (3) Deaths among the different age and sex groups

b. Morbidity:

   (1) Incidence of disease--chronic bronchitis, pulmonary emphysema, diffuse interstitial pneumonitis, cancer of respiratory tract, disease of remote organ (e.g., gastro-intestinal, ophthalmic, and cardiovascular systems)

   (2) Prevalence of diseases--same examples as for "incidence"

   (3) Prevalence of respiratory symptoms (e.g., changes in

quality and/or quantity of sputum production)

   (4) Exacerbation of diseases--rhinorrhea, asthma, tracheobronchitis, and chronic illness and enhancement of infection: pneumonia, sinusitis, otitis, mastoiditis

   (5) Changes in clinical conditions (e.g., bronchitic patients)

c. Changes in various aspects of lung function:

   (1) Ventilatory function--decrease in peak flow rate, decrease in spirometric volumes, impairment of flow-volume relationships, and increased airways resistance

   (2) Blood/gas distribution--impairment of lung-gas distribution

   (3) Blood/gas exchange--impairment of pulmonary blood-gas exchange

   (4) Increased work of breathing

Definitions of the various disease states are to be found in the glossary; most of the pulmonary function methods have been mentioned in Chapters 9 and 10 of the companion document, Air Quality Criteria for Particulate Matter.

The manner of presentation of the state of epidemiological knowledge of effects of sulfur dioxide in the ambient atmosphere when accompanied by particulate matter is outlined in the Table of Contents.

2. Cautions

In the first place, methods of measurement vary from country to country and place to place. Results from the various methods of measurement are frequently very dissimilar.

Secondly, pollution and health indices are not always measured over the same time periods. It is to be hoped that the pollution levels cited bear some relation to those extant during the time when the chronic disease states were developing. Further, acute effects require frequent short-term pollution measurements to enhance detection, while long-term chronic processes may be adequately related to long-term sampling intervals. Air pollution measurements useful in studies of acute health effects are becoming available; a less satisfactory situation exists for the long-term effects studied.

Thirdly, in many instances the possible role of cigarette smoking has not been considered. It is expected that future epidemiologic studies involving adults will routinely collect data on smoking habits of the study group. Other factors are significantly related to respiratory disease. These include occupational and other past exposures; infections, past and present; and allergy and heredity.

Few or no epidemiologic studies have been possible where the pollution challenge has been limited to oxides of sulfur, unaccompanied by significant amounts of other pollutant substances. Indeed, most of the available conclusions link sulfur dioxide levels with those of concurrently measured particulate matter; some studies attempt statistical separation of the culpability of one factor from the other in the effects cited.

In seeking the possible effects on populations resident in areas of differing air pollution, factors such as smoking, type and conditions of employment, ethnic group, and mobility in response to experienced irritation or disease have sometimes been considered. There has, however, been a minimum of attention paid to the indoor or domestic environments and their potential contribution. Measurement of such indoor exposures might be difficult, but omission of the information could well modify the appraisal of the importance of pollution by the oxides of sulfur.

Toxicologic studies indicate a specific potential of some oxides of sulfur to produce human responses. The levels used in toxicologic studies are far higher than those found in the communities in the epidemiologic studies under review. Thus the actual responsibility of oxides of sulfur for the community responses is uncertain, and it is sometimes necessary to invoke additional concepts; for example, the idea of synergism with other known or unknown ambient pollutants, or the idea that sulfur dioxide is but an index of availability of some other substance(s) which are fully responsible for the effects reported.

Over a short period of time, mortality fluctuates considerably, and only a systematic, long-term approach will allow a valid determination of the real role of air pollution. Cassell et al.[2] have reviewed the problem of detecting peaks in mortality and relating them to any single variable. The danger with episodic studies is that short-term fluctuation in the death rate, when picked to coincide with an air pollution incident, may appear to be causally related; in the long term, however, numerous other unassociated peaks are found in both the death rates and the air pollution levels.

The concept of "susceptible population" demands consideration. Human responses to toxicants, and to community air pollution, show wide variations, which contribute in no small way to the difficulty in assessing in a general manner the effects of pollutants. Since air quality criteria must, unless otherwise specified, consider "all" population rather than just major segments of it, studies must consider especially the impact of air pollution on the "most sensitive" responders. Many factors seem to enhance susceptibility or sensitivity to air pollution. These include being at the extremes of age, (i.e., infants and the very old); having preexisting chronic respiratory disease (e.g., pulmonary emphysema or chronic bronchitis); having preexisting cardiovascular disease (functional capacity not defined); regularly smoking cigarettes; or living in overcrowded or depressed socioeconomic strata. Some of these factors have been singled out for attention in the references to be cited, and the level of pollutant said to have an "effect" may take cognizance of such special sensitivity.

The effects discussed are related insofar as possible to specific pollution over specific time intervals; it must be emphasized that lower values by no means imply a "no effect" level of the pollutants.

C. INDICES OF HUMAN RESPONSE: THE EPIDEMIOLOGIC STUDIES

1. Acute Episodes

a. Mortality

The first well studied air pollution episode occurred between December 1 and 5, 1930, in the Meuse Valley, Belgium, when a heavy fog covered the entire valley. Several hundred people were severely ill with respiratory symptoms and 63 died. Although no precise measurements were made during the episode, Firket estimated that a number of pollutants rose to high levels and that sulfur dioxide and sulfuric acid, which may have reached a total of 25 mg/m^3 or higher (about 9ppm), were probably the chief cause of the illness.[3,4]

During late October 1948, Donora, Pennsylvania was blanketed by a dense fog, and 43 percent of the population was affected to some degree. Twenty persons died during or shortly after the smog, and 10 percent of the population was classified as severely affected. No measurements were taken during the episode, but a detailed study afterwards[5] concluded that no single agent was responsible, and that the observed effects were due to a chemical agent together with particulate matter. Sulfur dioxide and its oxidation products were undoubtedly significant contaminants. During subsequent inversion periods, presumably not as severe as the one in October 1948, daily averages of sulfur dioxide as high as 1.1 mg/m^3 (0.4 ppm) were recorded.[5]

In writing about the Meuse Valley episode in 1936, Firket stated that if there were a similar phenomenon in London, some 3200 deaths might occur. Unfortunately he was quite accurate in his estimate since, in December 1952, the world's most disastrous smog incident occurred in London, causing about 4000 excess deaths throughout the Greater London area. Marked increases were noted in both respiratory and cardiovascular deaths (and for almost every cause except traffic accidents; presumably the smog was too thick for people to drive). Since some of the diseases such as lung cancer and tuberculosis were obviously existent before the pollution episode, much of the effect of the fog was clearly to hasten the death of people who were already ill. Detailed investigations were made of 1,280 post-mortem reports of persons who had died before, during, or shortly after the episode. No fatalities were found which could not have been explained by previous respiratory or cardiovascular lesions. In this episode as in others, the elderly and persons with preexisting pulmonary and cardiac disease were most susceptible.

The maximum daily concentration of sulfur dioxide recorded during the 1952 London smog was 4 mg/m^3 (1.34 ppm)* which appeared on the third and fourth day of the fog. Corresponding smoke levels were 4.46 mg/m^3. These figures are from County Hall, where only volumetric (hydrogen peroxide) measurements of SO_2 were made.[6]

Greater London has had several air pollution episodes before and since the large one of December 1952, but none has come close to causing 4,000 excess deaths.

A number of investigations have analyzed and compared the various London episodes. The report by Brasser et al.[7] appears to cover all the episodes and to present a relatively detailed analysis of each of these episodes, pointing out the importance of the duration of the maximum values. More recently, Joosting[8] has examined the relationship between the duration of maximum values of sulfur dioxide and smoke during air pollution episodes, as well as the differential relationship between sulfur dioxide and smoke levels and the resulting mortality.

In conurbations, such as London, New York, Chicago, and Detroit, it has been possible to observe deviations from the moving averages of deaths during various seasons, and to relate such deviations to the coincident period levels of air pollutants.[9]

Gore and Shaddick[10] and Burgess and Shaddick[11] reviewed acute "fog" episodes which occurred in London in 1954, 1955, 1956 (January and December), and 1957 (December), in terms of excess mortality above a moving average, related to the mean of daily readings at seven stations

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*Unless otherwise stated, British measurements of sulfur oxide concentrations are obtained by the hydrogen peroxide titrimetric method and may be higher than the actual sulfur oxide concentration due to the presence of other acidic gases.

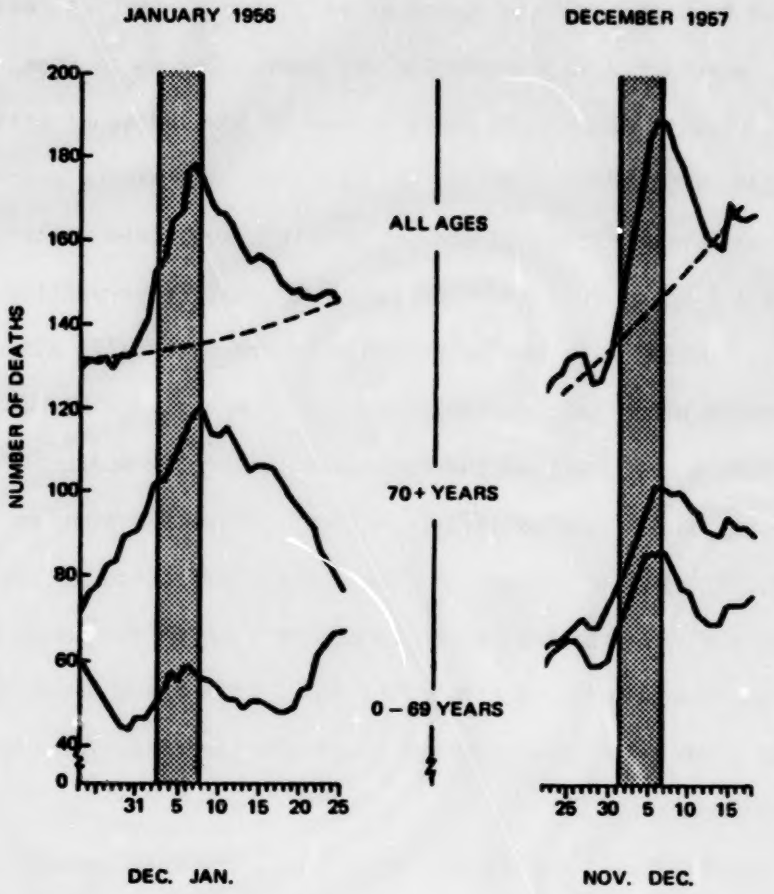

Figure 8-1. Mortality figures for the January 1956 and December 1957 smog "episodes" in London.[11] (The figure shows the increase in numbers of deaths during smog "episodes" (shaded periods), especially in the older age group.)

for smoke and SO_2. Figure 8-1 shows mortality figures for the January 1956 and December 1957 episodes. Somewhat differing patterns of onset of mortality rise, of age of population suffering most heavily, of deaths related to bronchitis and to other respiratory diseases, and of total deaths, were noted in these acute episodes. Common to them, however, were elevations of mean daily levels of SO_2 and smoke measured at seven different stations from two to four times the winter average levels; "effects" were estimated at 2 mg/m^3 black suspended matter together with 1.1 mg/m^3 (0.4 ppm)* of sulfur dioxide (representing all acidic gases). Deaths ascribed to bronchitis were materially affected, but deaths due to other causes also increased. Deaths appeared to begin to increase before the onset of the episodes; during the episodes, of course, they increased substantially. Scott[12] observed a similar relationship, for similar periods of "fog," with "effective pollutant" levels at seven different stations in London of 2 mg/m^3 for smoke and 0.4 ppm for SO_2 (reported by Scott as 1.1 mg/m^3).** There was a sharp impact on the elderly and the greatest proportionate rise, for cause of death, was in bronchitics.

Martin and Bradley[13] correlated daily mortality (all causes) and daily bronchitis mortality with mean daily black suspended matter for the winter of 1958-1959, and also found a significant positive association between mean daily sulfur dioxide levels and deaths (all causes). Bronchitis deaths showed a lower correlation with the pollution level, and the authors suggest the need for consideration of effects of air pollution on patients with cardiovascular disease. In addition, excess deaths have been related to increases (on the day preceding death) of mean daily black suspended matter by more than 0.2 mg/m^3, and rises in mean daily SO_2 of more than about 75 μg/m^3 (0.025 ppm).* In a later paper[14], data are shown to suggest an increase in mortality from all causes, and of respiratory and cardiac morbidity, associated with levels of smoke about 1 mg/m^3, and SO_2 concentrations of 0.72 mg/m^3 (0.25 ppm). This "effect" is properly related to abrupt rises in the concentrations of smoke and/or SO_2, with perhaps a continuum of effects at lower levels. Since these measurements were obtained at a single point in Central London, it should be presumed that a relatively wide range of values around these levels actually contributed to the mortality statistics which were correlated. A re-analysis by Lawther[15] of these mortality studies places the mortality "effect" at about 0.75 mg/m^3 for smoke and 0.715 mg/m^3 (0.25 ppm) for SO_2. Joosting[8] states that the maximum sulfur dioxide concentration above which significant correlations occur with death and disease is 0.4 to 0.5 mg/m^3 (0.15 to 0.19 ppm)** when there is a high soot content.

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*SO_2 values in this study were originally reported in ppm.

**SO_2 is converted from ppm to mg/m^3 in Scott's report by using an equivalency 2.85 mg/m^3=1 ppm. This report uses 2.86 mg/m^3=1 ppm, and for consistency attempts to express the value (0° C, 760 mm Hg) in mg/m^3 first. Most of the American SO_2 values are measured at 25° C, 760 mm Hg; the equivalency under these circumstances is 2.6 mg/m^3=1 ppm.

The Dutch report on sulfur dioxide[7] which discusses in detail seven air pollution episodes in London, states that in the December 1956 episode, 400 excess deaths, or 25 percent above expected, were observed in Greater London at maximum 24-hour levels of 1.2 mg/m^3 for smoke and 1.1 mg/m^3 for SO_2 (0.4 ppm).* The report also notes that in January 1959, 200 excess deaths were observed in Greater London, or 10 percent above the expected mortality, at a level of 1.2 mg/m^3 for smoke and 0.80 mg/m^3 (0.30 ppm)* for SO_2. The episodes all took place during winter; cold weather seems to be an important factor in London air pollution mortality.

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*SO_2 values in this study were originally reported in parts per billion (ppb).

**SO_2 is converted from ppm to mg/m^3 in the Dutch reports by using the equivalency, 2.7 mg/m^3=1 ppm. This report uses 2.86 mg/m^3=1 ppm whenever possible.

In Martin's review[14] in 1964 of daily mortality in London during the winters of 1958-1959 and 1959-1960, he concluded: "From the data it would be difficult to fix any threshold value below which levels of air pollution might be regarded as safe." However, his review included data with sulfur dioxide concentrations ranging upward from about 0.4 mg/m^3 (0.14 ppm) and smoke concentrations of 0.5 mg/m^3 and above.

As a result of smoke control regulations, the particle content of London air has steadily decreased since the 1950's but the sulfur dioxide concentrations have not decreased proportionately. At the same measuring sites as in 1952, sulfur dioxide was actually slightly higher in the 1962 episode than in that of 1952, but smoke levels were considerably lower. Also, as Brasser et al. have noted, there was only one day of maximum pollution values in 1962 as contrasted with the two days of maximum pollution in December 1952.[7] Since 1952, a great deal of publicity has been given to the harmful effects of smog, and more susceptible individuals have been encouraged to use masks and filters and stay indoors. In addition, when episodes come close together, a large number of susceptible individuals might not accumulate, since some are killed off each time. An effect as large as that seen in the first incident would not, therefore, be expected.

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*SO_2 is converted from ppm to mg/m^3 in the Dutch reports by using the equivalency, 2.7 mg/m^3=1 ppm. This report uses 2.86 mg/m^3=1 ppm whenever possible.

The number of deaths in New York City was reviewed for excess mortality in relation to the air pollution episode of November 1953 by Greenburg et al.[16] Excess deaths were related to elevations of concentrations of sulfur dioxide and suspended particles. Average daily smoke shade measured in Central Park was in excess of 5.0 coh units, while the SO_2 rose from the New York City average ranges of 0.43 to 0.57 mg/m^3 (0.15 to 0.20 ppm) to a maximum level of 2.5 mg/m^3 (0.86 ppm), probably a half-hour value. For this episode, there was a "lag effect," and distribution of excess deaths among all age groups was noted. The number of deaths, although not showing the marked rise seen in some of the London episodes, was above average for comparable periods in other years during and immediately after the incident. For the November 15 to 24, 1953, period, the average number of deaths per day was 244, whereas during the 3 years preceding and following 1953, the average was 224 deaths per day for the same calendar period.

A later episode (1962) was studied, but Greenburg et al.[17] did not discern an excess mortality. However, McCarroll and Bradley,[18] reviewing episodes in New York City in November and December of 1962, January and February of 1963, and February and March of 1964, compared 24-hour average levels of various pollutants with New York City mortality figures, employing daily deviations from 15-day moving average; the measurements were performed at a single station in lower Manhattan, and fluctuations in the values at this station were known to correlate well with those at another station 10 km away. Excess deaths on December 1, 1962, followed a daily average sulfur dioxide concentration of 2.6 mg/m^3 (0.72 ppm) and smoke shade in excess of 6 coh units, during a period of atmospheric inversion and low ground-wind speed. The increased death rates were shared by the 45 to 64 age group, as well as by the age group over 65. In a later episode, January 7, 1963, associated with an SO_2 concentration of about 1.7 mg/m^3 (0.6 ppm) and a smoke shade value of 6 coh units, there was a peak death rate apparently superimposed upon an elevated death rate average due to the presence of influenza virus in the community.

Another severe episode of air pollution encompassed the New York City area during the Thanksgiving weekend, November 23 to 25, 1966. The maximum 24-hour average of hourly SO_2 values was 1.46 mg/m^3 (0.51 ppm) (electroconductivity) on November 23, and 1.34 and 1.18 mg/m^3 (0.47 and 0.41 ppm) on the 24th and 25th. The maximum hourly concentration was 2.92 mg/m^3 (1.02 ppm). Smoke shade values were above 5 cohs on the 3 days. The average number of daily deaths during the 7 days of the air pollution episode was 261 compared to the expected value of 237 for control periods in 6 surrounding years.[19]

An example of the inherent danger of relating mortality peaks to air pollution is shown by Leonard et al.[20] in the Dublin studies. During the war and postwar years of 1941 to 1947, peat was burned as the main fuel rather than coal, and air pollution (as measured by particle concentrations) was markedly decreased. Sulfur dioxide levels varied in a manner similar to those of suspended particulate matter. The winter peaks in death, however, were unaffected, and thus do not seem to be related to air pollution. When coal again became available in 1948, the

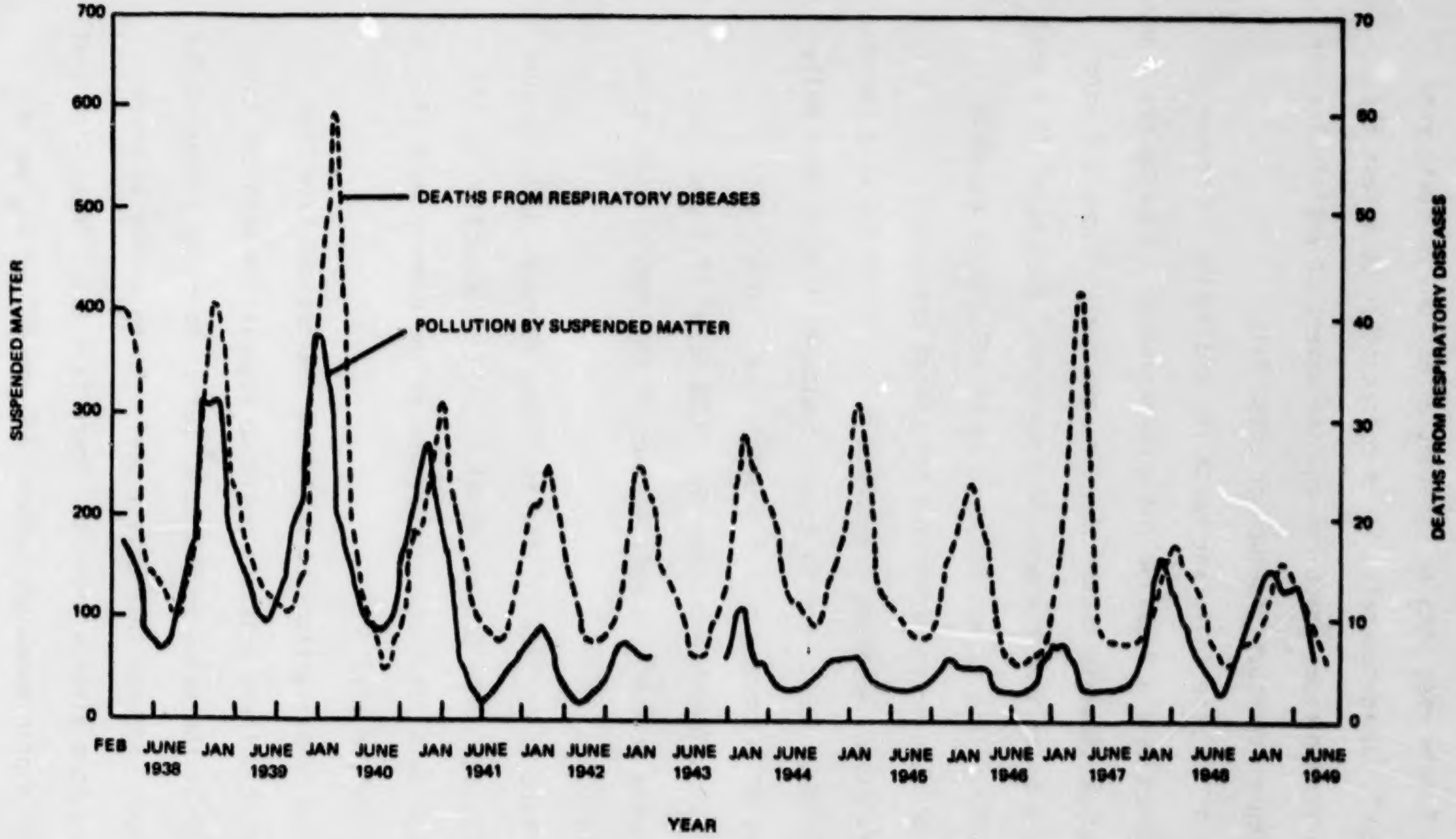

Figure 8-2. Death rates and air pollution levels in Dublin, Ireland, for 1938-1949.

air pollution levels rose with no apparent effect on the death rate (see Figure 8-2). Unfortunately, it is not possible to assess the effect of changing medical practices and the advent of antibiotics for use in treating respiratory diseases on these data.

In Detroit[21] a rise in infant mortality and deaths in cancer patients occurred over a 3-day period accompanied by a rise in the 3-day mean suspended particulate matter for the same period above 0.2 mg/m^3 and accompanied by an instantaneous SO_2 maximum of 2.86 mg/m^3 (1.0 ppm) (September 1952). This is not believed to be related to the cold temperatures which have characterized the London episodes.

In Osaka, Japan, Watanabe[22] reported on excess deaths in a December 1962 smog episode. There were 60 excess deaths related to mean daily concentrations of suspended matter greater than 1 mg/m^3, with accompanying sulfur dioxide greater than 0.28 mg/m^3 (0.1 ppm); the measurements were made at a single station in the central commercial area of the city.

In an effort to include all the available relevant data, we must mention the discussion by Brasser et al.[7]; calling attention to the availability of data for Rotterdam because of the pioneer work of Bierstecker, Brasser says:

> "From investigations at Rotterdam indications have been obtained that there exists a positive association with the total mortality if the value of 500 $\mu g/m^3$ per 24 hours is surpassed for a few days. Perhaps this effect begins to be active at lower concentrations already present. There is a faint indication that this will happen somewhere between 300 and 500 μg SO_2 per m^3 per 24 hours."

The Rotterdam episodes of January-February 1959 and December 1962 have also been discussed by Joosting.[8] What is especially significant is that particulate levels are generally low in Rotterdam. On comparing particulate and SO_2 concentrations, Joosting has characterized the ratio of particulates to SO_2 as 1:1, 1:1.5 to 1:2, and 1:3 to 1:4. Rotterdam is in the last category, whereas London is in the first. Measurements in Rotterdam are made with the hydrogen peroxide titrimetric method.

When a marked increase in air pollution is associated with a sudden dramatic rise in the death rate or illness rate lasting for a few days and both return to normal shortly thereafter, a causal relationship is strongly suggested. Sudden changes in weather, however, which may have caused the air pollution incident, must be considered as another possible cause of the death rate increase. Over the years, a number of such acute episodes have been reported, and there seems little doubt that air

Table 8-1. SURVEY OF SELECTED ACUTE AIR POLLUTION EPISODES IN GREATER LONDON[7]

	Dec. 1952	Jan. 1956	Dec. 1962	Dec. 1957	Dec. 1956	Jan. 1955	Jan. 1959
Duration of the cumulation period in days	5	5	5	5	10	11	5
Number of days with maximum pollution	2	2	1	1	5	1x3[a]	1
SO_2 level preceding episode	500	300	400	300	300	300	300
SO_2 maximum	4000	1500	3300	1600	1100	1200	800
SO_2 increase per day	1200	500	1000	325	400	450	250
Soot level preceding episode	400	500	200	400	400	500	400
Soot maximum	4000	3250	2000	2300	1200	1750	1200
Soot increase per day	1200	1300	600	500	400	600	400
Number of excess deaths	3900	1000	850	800	400	240	200
Number of days with excess mortality	18	10	13	10	6	6	6
Daily mortality expected under normal circumstances	300	330	310	300	270	320	325
Average daily mortality in the period (excess mortality as a percent of normal)	170	130	120	125	125	112	110

Remark: The SO_2 and soot concentrations mentioned are average values over 24 hours expressed in μg/m³.

[a] Maximum pollution values of one day's duration occurred three times.

pollution was the cause.

Table 8-1 is an attempt by Brasser et al.[7] to summarize some of the recent major air pollution episodes in Greater London.

The British studies presented in this section suggest that excess mortality, a small rise in the daily death rate, is detectable in large populations if the concentrations of sulfur dioxide rise abruptly to levels at or about 0.715 mg/m^3 (about 0.25 ppm) in the presence of smoke at 0.75 mg/m^3. The major targets are the aged population, patients with chronic obstructive pulmonary disease, and patients with cardiac disease. A more distinct rise in deaths is noted generally when sulfur dioxide exceeds 1 mg/m^3 (about 0.35 ppm) for 1 day and particulate matter reaches about 1.2 mg/m^3. Daily concentrations of sulfur dioxide in excess of 1.5 mg/m^3 for 1 day (about .5 ppm) in conjunction with levels of suspended particles exceeding 2.0 mg/m^3 appear to be associated with an increase in the death rate of 20 percent of more over base line levels. This same effect is observed at lower sulfur dioxide levels if the maximum pollution levels last for a longer period.

b. Morbidity

The acute episodes have resulted in substantial increases in illness. Thus a survey[23] of emergency clinics at major New York City hospitals in November 1953 indicated a rise in visits for upper respiratory infections and cardiac diseases in both children and adults in all of the four hospitals studied. Sulfur dioxide ranged between 0.2 and 2.460 mg/m^3 (0.07 to 0.86 ppm) during the period from November 12 to 24, and hospital admissions were clearly elevated by November 16, at which time concentrations had not yet exceeded 0.715 mg/m^3 (0.25 ppm); "smoke shade" at this time was close to 3 coh units.[16]

Again, the number of emergency clinic visits for bronchitis and asthma at seven large New York City hospitals was examined during the Thanksgiving 1966 air pollution episode.[24] There was a rise in the number of such visits on the third day of the episode, among the patients aged 45 and over, at three of the seven hospitals investigated. Unfortunately, the Thanksgiving holiday greatly complicated evaluation of the emergency clinic visits over the holiday period.[19]

In the investigation of the London episode of December 1952, information on illness was collected from as many sources as possible including sickness claims, applications for hospital admission, pneumonia notifications, and records of physicians. The analysis demonstrated a real and important increase in morbidity, though there was some indication that the increase in illness was not as large proportionately as the increase in deaths and the effects were not so sudden in producing a marked rise in the early days of the episode. In a number of other severe London episodes the increase in morbidity put a considerable strain on the health services.

These episodes reflect results which fall into Level IV of the World Health Organization's "guides to air quality."[25] These "guides," equivalent in usage to our term "criteria," cover sets of concentrations and exposure times at which specified types of effects are noted or at which no effect is noted. Level IV includes "concentrations and exposure times at and above which there is likely to be acute illness or death in susceptible groups of the population."

2. Chronic (Long-Term) Air Pollution

Kurland[26] has called to our attention the fact that the air pollution episodes represent, by definition, episodes of massive, overwhelming, and unusual exposure, and thus the most significant pathologic effects. There is an "iceberg" effect in that such data represent the obvious, while the greater share of the problem remains submerged. We are dealing with an essential dose-response situation, the upper limits of which are represented by these episodes.

a. Day-to-Day Variations in Mortality and Morbidity

In a systematic approach to analyzing respiratory and cardiac morbidity daily in London, Martin[14] examined deviations in morbidity from a 15-day moving average in London during the winters of 1958-1959 and 1959-1960. Both smoke and sulfur dioxide concentrations appear to be about equally related to morbidity rates, and a definite excess in morbidity seemed to exist as it did for mortality, though there was a somewhat greater degree of irregularity.

An approach similar to Martin's, but limited to observations on mortality, was used by McCarroll and Bradley[18] in New York City. Covering a 3-year period (1962-1964) they examined a number of peaks in New York City mortality associated with periods of high air pollution. There are examples given where sulfur dioxide and smoke shade appear to be related to mortality. The authors present other episodes, however, where the relationship to air pollution is not nearly as clear, although the death rate fluctuates to even higher peaks. Reference to this analysis has already been made in our discussion of the data on episodes in Section B-1.

The rate of hospital admissions, obtained from data collected by a medical insurance group, was used by Sterling et al.[27] to study the effects of air pollution on hospitalization of about 10,000 individuals in Los Angeles. Certain diseases considered to be relevant to air pollution, such as allergic disorders, inflammatory disease of the eye, acute upper respiratory infections, influenza, and bronchitis, were found to be related to daily concentrations (measured as daily average minimum and maximum values) of oxidants, carbon monoxide, sulfur dioxide, oxides of nitrogen, ozone, oxidant precursor, and particulate matter. Measurements were taken at eight different stations 8 to 16 kilometers apart from March to October. The analyses showed significantly larger admission rates on those days among the highest third of sulfur dioxide pollution than on those days among the lowest third. Sulfur dioxide concentrations during the period of the sutdy averaged less than about 45 $\mu g/m^3$ (0.015 ppm). Concentrations on days of highest pollution were not reported. The method of analysis generally is new and complex, and the author noted the need for additional time periods to be studied to take into account the possibility of seasonal variations. The analysis must also be extended to other cities.

McCarroll et al.[24] studied residents of a New York City housing project, using weekly questionnaires. Exact levels of sulfur dioxide which could be used for establishment of air quality criteria were not given; however, the data indicate that sulfur dioxide rather than particulate matter was associated with eye irritation. Symptoms of cough were also shown to be related to air pollution but were not well differentiated between association with particles and sulfur dioxide. The particular time-series analysis used with these data is not well known, and the biases inherent in its use have not been fully determined.

Results also obtained at Rotterdam have shown that when the SO_2 concentration rose for 3 to 4 days from about 0.3 to 0.5 mg/m^3 (0.11 to 0.19 ppm), the number of admissions into hospitals for respiratory tract "irritation" rose, especially in older individuals.[7]

Hodgson,[28] in analyzing 2.5 years of air pollution and mortality data in New York City for the period November 1962-May 1965, concluded that if the variation in mortality figures can be attributed to air pollution as reflected by particulate matter and SO_2 data, then slight or moderate increases in concentration of air pollution during a month can be expected to result in increased mortality from heart and respiratory diseases amounting to several hundred deaths in the New York City population. He notes that this is occurring at levels of pollution that are not considered unusually high.

Cassell et al.[29] analyzed illness records of 1747 persons in New York City for an average of 45 weeks (giving 61,000 person-weeks of information) and concluded that the effect of air pollution is greater than the sum of the effects of the individual air pollutants. His conclusions were that the mechanisms of adverse health effects during air pollution are still obscure and that present-day epidemiological studies represent a primative stage of knowledge because of the multifactor effects in a problem of this scope.

Glasser and Greenburg[30] analyzed daily deaths in New York City for the years 1960-1964 in relation to SO_2, smoke shade, temperature deviations from normal, wind speed, sky cover, and rainfall. In their studies SO_2 level was shown to be more strongly related to mortality than was smoke shade. This correlation appeared to be independent of the weather factors studied. They estimated that the difference in mean number of daily deaths on days with 0.6 mg/m^3 (0.20 ppm) or less mean SO_2 concentration compared to days having mean SO_2 concentration of 1.2 mg/m^3 (0.40 ppm) was 10 to 20 deaths per day.

b. Geographical Variations in Mortality

(1) Studies Based on Available Data. Mortality and morbidity statistics each have advantages as well as disadvantages. Records of illness should be more fruitful in defining subtle effects, since illness precedes death and since all illness does not result in death. Mortality statistics are collected in every country and are available for quick tabulation. Unfortunately, the quality of mortality statistics varies. One of the problems is that, with the present system of tabulating mortality data, a single cause of death must be selected and coded, even though more than one cause may be involved in the death. The single cause of death designated (e.g., specific chronic respiratory disease) depends largely on the judgment of the attending physician and has little, if any, relation to epidemiologic use. While contributing causes of death appear on the death certificate, they are not reflected in summary tabulations. The coding of only the "underlying" cause of death minimizes the importance of such diseases as emphysema which often appear on the death certificate as contributory or associated causes of death.[31]

Almost all studies of the effects of long-term exposure on death rates compare the rate in one area with that in another. Mortality as well as morbidity studies are hampered by the possibility of differences other than air pollution existing between the areas, such as social class, occupation, age, and sex composition of the population, and cigarette smoking. Assuming that almost all deaths are recorded and tabulated, comparison of total mortality rates (i.e., deaths from all causes) obviates the bias of diagnostic selection, but does not lessen the chances of other associated factors having caused the difference.

Buck and Brown[32] reported in 1964 the relation of standardized mortality ratios for the 5-year period 1955-1959 to four variables: daily smoke and SO_2 concentrations for March 1962 (presumed representative of the study period), population density in 1961, and a social index of 1951. The studies involved populations in 214 areas of the United Kingdom (19 London boroughs, 40 county boroughs, 70 other boroughs, 61 urban districts, and 15 rural districts).

Statistical analysis indicated that bronchitis mortality had a significant positive association with both the smoke and SO_2 concentrations encountered in these residential areas, and also with social index. The standardized mortality rates for lung cancer were not, in general, significantly associated with smoke or SO_2 concentrations in the residential areas. Examination of the tables given by Buck and Brown suggests that the excess of bronchitis mortality occurred for classes of area where the average daily smoke and SO_2 concentrations both exceeded 0.2 mg/m^3 (0.07 ppm). Although smoking habits were reviewed and were apparently uniform from area to area, occupational and domestic indoor environmental exposures were not considered. The pollutant values selected for the correlations did not cover the same time periods as the mortality figures. The associations of bronchitis mortality with smoke and sulfur dioxide were about equal, and the effects of the two pollutants cannot be separated. Variations in smoking habits did not seem to account for much of the mortality variation.

In addition to studies of acute variations in mortality in relation to air pollution indices, Burgess and Shaddick[11] studies mortality rates in London and their relationship to smoke, sulfur dioxide, social class, and place of birth (in or out of London). Average levels of sulfur dioxide did not vary much among the areas, ranging from 0.19 to 0.315 mg/m^3 (0.07 to 0.11 ppm); sampling was performed at seven widely scattered points every 24 hours during normal winter weather and every 4 hours during fog periods. A significant relationship between lung cancer or bronchitis mortality and smoke or sulfur dioxide was not demonstrated. Births in London and low social class (occupational stratification) were both associated with higher rates. The differences in sulfur dioxide levels are small among the different areas, and it is difficult to believe that, even if sulfur dioxide were a fairly strong causal factor, any significant differences could be shown by this method. What appear to be the same data, slightly rearranged, are reported by Gore and Shaddick[10] with the same basic conclusions.

In a similar study carried out a few years prior to the above, Pemberton and Goldberg[33] compared bronchitis death rates in persons over age 45 in 33 county boroughs of England and Wales for which air pollution data were available. Two indices of social conditions were used: (1) the number of persons per room, and (2) an estimated percentage of households with income exceeding a certain level. Counties from urban and industrial areas were included. Significant correlations were found with bronchitis death rates and sulfur dioxide pollution, but not with "total solids." The association was true for male but not for female bronchitis rates. No significant correlation was found between the two indices of social class and sulfur dioxide pollution. No evidence was given for smoking differences, and no specific sulfur dioxide levels were given that would allow establishment of ambient air quality.

Gorham[34] found a correlation between the crude pneumonia death rate and atmospheric sulfate deposits in the 53 counties of England and Wales. The original data were not given, and the rates were not corrected for age differences or social class; the study can therefore only be suggested until confirmed by more accurate methods.

Other studies[35,36] have confirmed an association in Great Britain of bronchitis death rates with general indices of air pollution, and an equally strong association in general holds up when various measures of social class are held constant by statistical means. Lung cancer mortality is consistently associated with measures of population density and cigarette smoking, but not with general indices of air pollution.

Watanabe and Kaneko[37] studied the relationship during the period November 1962-October 1967 between number of daily deaths and air pollution in Osaka City. The area of Osaka Prefecture was divided into three areas: (1) suburban-industrial, (2) suburban-residential, and (3) Osaka City. In his studies it was concluded that the increase in number of deaths in the city area is affected independently by air pollution concentration, degree of increase of air pollution, and cold. The variation of number of deaths was found to be affected more by SO_2 concentration than by the suspended particulate. He further concluded that an SO_2 concentration of over 0.3 mg/m^3 (0.1 ppm) should be regarded as an index of unhealthy atmospheric pollution in a city area. These conclusions are not accepted by many epidemiologists.

Reichel[38] studying the relationship between air pollution and respiratory diseases in Western Germany, studied three districts with different levels of air pollution (SO_2 varied between 0.09 and 0.90 mg/m^3

and suspended particulates between 0.01 and 0.39 mg/m^3). He found no difference in prevalence of persistent cough and expectoration between men and women living in the different air-polluted areas, if the groups were standardized for age, sex, smoking habits, and social customs, and that there was no evidence that community air pollution in limited levels leads to impairment of the lung mechanics of gas exchange.

In the report on air pollution and its effect on health by the Committee of the Royal College of Physicians of London,[39] it was pointed out that all investigations in Britain have demonstrated a close correlation between levels of pollutants in the air and mortality from bronchitis in middle age. For example, among postmen, rates of disablement, absence from work, and premature death from bronchitis were high in the most polluted areas. Highest rates of disability among postmen and bus drivers were in the center and northeast of London where air pollution was highest.

(2) Special Studies Involving the Collection of New Data. In 1964, also, Wicken and Buck[40] reported on a study of bronchitis and lung cancer mortality in six areas of Northeast England, one in Eston, another in Stockton and four in rural districts. The deaths covered the period 1952 to 1962. The survey of decedents with cause of death from bronchitis or lung cancer was matched against the survey of decedents with cause of death from nonrespiratory disease controlled for age and sex; the basis for the diagnostic classifications was not stated in the report. Personal interviews were carried out with next of kin. Personal interviews of a random sample of households were also conducted to obtain sex, age, smoking habits and occupation of the population at risk, the living population. The survey of decedents was carried out

between January and October 1963; the survey of the living population was carried out between December 1963 and March 1964. Smoke and sulfur dioxide concentrations were measured in the Eston urban district. One year's aerometric data were obtained. The study was excellent in principle though, unfortunately, sulfur dioxide and particulate values were available only for the Eston urban district.

Eston, itself, as a substudy, was subdivided into north Eston and south Eston. North Eston contains or lies near heavy industrial plants, whereas south Eston is a residential area. During the period May 1963 to April 1964, mean weekly observations of the sulfur dioxide and smoke concentrations were carried out in two sites in north Eston and one station in south Eston. The sulfur dioxide value in north Eston on the yearly average was 0.12 mg/m^3 (0.040 ppm) and for south Eston it was 74 μg/m^3 (0.026 ppm). Smoke values were 160 and 80 μg/m^3 for north and south Eston respectively. The deaths studied occurred between 1952 and 1962. Adjustments were made for differences in age composition, smoking habits and social class, and these were insufficient to explain the differences in lung cancer and bronchitis mortality rates between the two localities. Occupational exposure to pollution was then taken into account in the analysis. The conclusion was that there is an association between the degree of air pollution and the incidence of lung cancer and bronchitis mortality in the two areas of the Eston urban district. Though both sulfur dioxide and smoke values and concentrations are furnished in the report and the effects apparently cannot be separated, Brasser et al.[7] apparently have used the sulfur dioxide concentration as the more relevant measure of this study.

In a later study by Burn and Pemberton[41] the community of Salford

Table 8-2. POLLUTION LEVELS IN SALFORD (SEASONAL DAILY AVERAGES)[41]

Pollution area classification	Smoke, μg/m³		SO_2, μg/m³ (ppm in parentheses)		Deaths $\frac{\text{observed}}{\text{expected}}$ x 100		
	Winter	Summer	Winter	Summer	All Causes	Bronchitis	Lung Cancer
High	680	270	715 (0.25)	255 (0.09)	106	128	124
Intermediate	490	170	460 (0.16)	200 (0.07)	100	97	84
Low	450	170	340 (0.12)	145 (0.05)	90	52	79

Note: The data in the original report show SO_2 concentrations in parts per hundred million (pphm).

was classified into three pollution areas according to Table 8-2. Five sampling stations in the area were employed. Despite the closeness of the ranges of values, a high rate of bronchitis mortality, of lung cancer mortality, and of deaths from all causes, was observed in the high, compared to the lower, pollution wards. It appears (see Section C-4) that there was also an increased rate of bronchitis morbidity in the highly polluted wards.

Winkelstein et al.[42-44] divided the city of Buffalo into three zones based on a network of 21 air sampling stations operated for a 2-year period. The city was also divided by census tracts into five economic levels based on median family income reported from the U.S. Census. Although the method by which the air pollution zones were determined is not clearly described, in the high zone sulfation levels were greater than approximately 0.45, in the intermediate zone, 0.30 to 0.45, and the low zone less than 0.30 (all units mg/cm^2/30 days). Total mortality from all causes for men aged 50 and over showed no association with sulfation within each economic stratum. Deaths from chronic respiratory diseases, including asthma, bronchitis, chronic interstitial pneumonia, bronchiectasis, and emphysema, could be examined only for white males aged 50 to 69 because of insufficient numbers. Only in the second economic level (income \$5,175 to \$6,004) were there more than five deaths in each air pollution level. Within this income group a clear gradient in mortality for chronic respiratory disease was seen from low to high air pollution, with the biggest difference being that between the moderate and high pollution areas. In the first (i.e., lowest) economic level (income \$3,005 to \$5,007), mortality for chronic respiratory disease was higher in the "high" oxides of sulfur area than in the "intermediate" pollution area. No consistent gradient was found for lung cancer deaths.

As the authors point out, since the only association between sulfation and respiratory disease mortality was in the lowest economic classes (first and second classes), and these classes were likely to have increased occupational exposures to air pollution, the relationship might be due to an intervening occupational variable. However, Reid has called attention to the likelihood of air pollution affecting the lowest socioeconomic group most.[45] This may be ascertained by a study which can measure effects on the lowest socioeconomic group in low, moderate, and high pollution areas. As in most community studies the effect of differences in smoking habits was not known in the Buffalo study. Also, the study did not take account of the ethnic background of the decedents, although Winkelstein's analysis of mortality from gastric cancer as related to particulate levels attempted to do this.

Lambert and Reid[46] carried out a postal survey of a large sample of the British population (12,236 completed questionnaires out of 18,379 were returned) in the relations between smoking, air pollution, and bronchitis. They drew the conclusion that in the absence of smoking the influence of other pollutants in the air is small. They did suspect some interaction between these factors that results in especially high prevalence rates among smokers living in the heavily polluted areas. It was also noted that the urban/rural gradient in morbidity was more striking among men than women.

From an aerometric standpoint, one of the most extensive studies of variations in mortality and morbidity within a city was the work of Zeidberg et al. in Nashville, Tennessee.[47,48] Aerometric data were collected at 123 sampling stations in a grid across the city. An area of "high" SO_2 concentrations was defined which had a geometric mean annual 24-hour level of about 30 $\mu g/m^3$ (0.01 ppm) or more. The "low" SO_2 area had about 15 $\mu g/m^3$ (0.005 ppm) or less. The high sulfation area had 0.351 mg $SO_3/100\ cm^2$-day or more as an annual geometric mean. Areas of high, moderate, and low pollution were also defined by soiling index, annual dustfall, and suspended particulate matter. All codable deaths registered between 1949 and 1960 (32,067) were then distributed among census tracts rated according to high, moderate, and low pollution levels, and upper, middle, and lower economic classes, and then further coded by age, sex, race, and underlying cause of death. In the study, account was not taken of smoking habits of the deceased; also, the "middle class" group covered a relatively large segment of the decedents. Standardized mortality ratios (for total respiratory disease, and for pheumonia, influenza, bronchitis, emphysema, tuberculosis, and lung and bronchial cancer) were then related to the pollution indices obtained during 1959. The statistically significant mortality increases were those for all respiratory diseases related to sulfation and soiling; lung and bronchial cancer mortality, and bronchitis and emphysema mortality were not clearly related. "High" pollution in these studies for soiling referred to more than 1.1 coh unit/1,000 linear feet. A later paper[49] derived from the same study period analyzed infant and fetal death rates between 1955 and 1960. For white infant mortality, significant regressions were obtained for sulfation; dustfall (alone, or as an interaction variable) was the most frequently related variable.

In summary, the results of this analysis of long-term exposure studies indicate effects which would coincide with Level III of the World Health Organization's "guides to air quality."[25] Level III is defined as "concentrations and exposure times at and above which there is likely to be impairment of vital physiologic functions or changes that may lead to chronic diseases or shortening of life."

c. Geographic Variations in Morbidity--Special Studies

It has been postulated that the study of records of illness rather than mortality should be more fruitful in defining subtle effects, since morbidity is an earlier and more sensitive index of deviation from normal health. A much larger insult must presumably be given to the body to cause death than to cause illness. Routinely collected morbidity data are, however, not generally available. Data may occasionally be obtained from group insurance plans, hospital admission records, or existing school records. Since such data are usually not collected in a uniform, precise manner, most morbidity studies require expensive and time-consuming field surveys with questionnaires or actual medical examinations of the subjects.

Morbidity studies of adults involving long-term exposures are frequently not as useful as desired, due to the presence of complicating factors such as occupation and smoking. Accordingly, Anderson has recommended[50] that children and housewives be used to determine the health effects of air pollution.

A study was conducted by Petrilli et al.[51] in Genoa, Italy, which followed Anderson's recommendation. This intensive survey of community respiratory morbidity was actually a set of epidemiologic studies to determine the air pollution effects in Genoa. The subjects studied in one of the research projects were women of 65 years of age, nonsmokers who lived for a long period in the same area and who had no industrial experience. Economic and social conditions in the areas of residence were considered as well as the levels of pollution in these areas of residence. Air pollution was monitored in Genoa for 10 years (1954-1964) at 19 sites covering the suburban area, the residential center, and the industrialized area. Sulfur dioxide was measured by a technique analogous to the volumetric method of the English Department of Scientific and Industrial Research. Carbon monoxide was also monitored. A retrospective survey was carried out using the M.R.C. questionnaire with slight modifications. As has been noted, several different epidemiologic studies appeared to have been conducted. Consideration was taken in the sample selection of age, length of residence in the same area, presence of cardiovascular disease, living habits, previous working habits, etc., in the design of the study. Morbidity indices were calculated for 1961 and 1962 for the population which received free medical care from the municipality and therefore was under continuous medical observation. Prevalence and incidence rates were calculated for symptoms such as cough, sputum, dyspnea, rhinitis, and recent and past respiratory diseases. The frequency of these respiratory symptoms was much greater in the central residential area than in the suburban residential area, even though the annual means of sulfur dioxide in the two areas were relatively close; the pattern for rhinitis was somewhat erratic.

Sulfur dioxide measurement in the cleanest area, that is, the suburban residential district, was 80 $\mu g/m^3$ (0.028 ppm) with the winter value being 85 $\mu g/m^3$ (0.030 ppm) and the summer value 55 $\mu g/m^3$ (0.019 ppm). The residential center area had an annual average value of 105 $\mu g/m^3$ (0.037 ppm), with a winter average of 115 $\mu g/m^3$ (0.040 ppm) and a summer average of 85 $\mu g/m^3$ (0.030 ppm). The industrial area averaged 265 $\mu g/m^3$ (0.093 ppm) for its annual mean with a winter average of 315 $\mu g/m^3$ (0.11 ppm) and a summer average of 230 $\mu g/m^3$ (0.080 ppm).

The study showed a striking correlation between frequency of symptoms and the diseases of the respiratory tract and air pollution levels. In the suburban residential area, the indices were almost always significantly lower for the data collected and particularly for the frequency of cough, sputum, dyspnea, rhinitis, and recent respiratory disease, especially bronchitis. There was usually a gradient between the suburban area and the industrial area. What was especially significant was the finding of differences generally in the prevalence of respiratory diseases during the summer in the industrial area as compared with the moderate and low pollution areas. This should contribute to our knowledge regarding the relationship between different climatic conditions and the health effects of air pollution.

It has been postulated that it is usually in the winter that air pollution of the reducing type exerts the most deleterious effects.

The study also examined a number of areas in the city. Data for the seven districts in the town of Genoa showed a very significant correlation (r=0.98) between the frequency of bronchitis and the annual mean of sulfur dioxide levels. A nonsignificant correlation between the frequency of bronchitis and suspended matter and dustfall was observed in the study. There was a suggested relationship between winter temperature and bronchitis, but this was further reduced when adjustment was made for air pollution.

What is particularly significant about this study is that the differences in respiratory disease were found between areas with an annual mean of 105 $\mu g/m^3$ (0.037 ppm) and one of 80 $\mu g/m^3$ (about 0.028 ppm). Also highly significant was the observation that effects of air pollution were found in the summer prevalence of respiratory disease. Very sharp differences were found within a community which is characterized by maximum sulfur dioxide levels below an annual average of 300 $\mu g/m^3$ (0.10 ppm). Finally, the very striking differences between the area with low levels of pollution and the industrialized areas were noted and should lend support to the results of studies in other areas.

Toyama,[52] in a comprehensive study of air pollution and its health effects in Japan, charted the age-standardized morbidity rates (per thousand) secured by interview survey in 1961, and described a gradient of respiratory disease morbidity from the highly industrialized (and presumably polluted) areas to the rural areas of Japan. Further, the pulmonary disease morbidity ratio was higher in the industrialized,

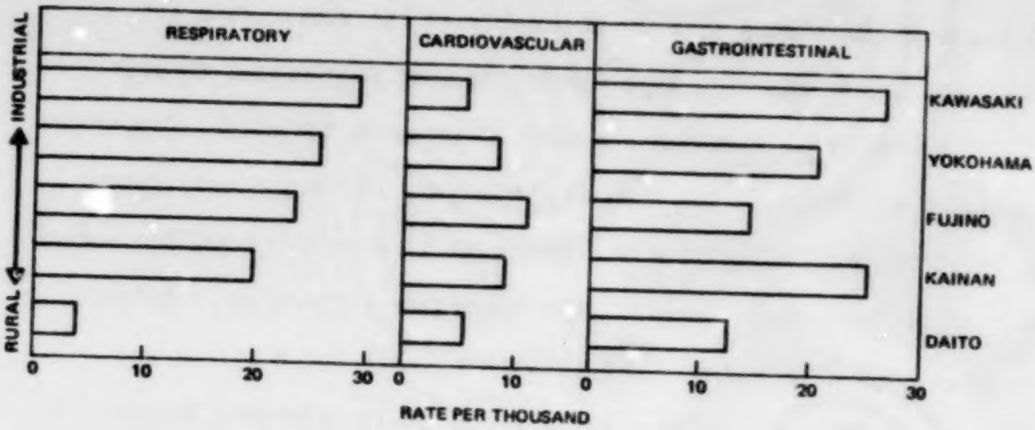

Figure 8-3. Age-standardized morbidity rate per 1,000 for three categories of diseases in Japan.[52] (The mortality rate for respiratory diseases shows a clear correlation with pollution levels; there is no such clear correlation for cardiovascular or gastrointestinal disorders.)

polluted areas than were the ratios for other disease groupings. This gradient was not noted for cardiovascular diseases nor for gastrointestinal diseases. Unfortunately, specific pollutant concentrations were not clearly indicated to accompany these data on morbidity. The age-standardized morbidity rates per thousand for several cities in Japan are shown in Figure 8-3.[52]

Pulmonary function and respiratory symptoms were compared in population areas of high (95 $\mu g/m^3$) and low (25 $\mu g/m^3$) SO_2 pollution (annual means of 0.034 and 0.009 ppm respectively) (measured by H_2O_2 absorption, H_2SO_4 titration) in Port Kembla, Australia.[53] Coh values in the more polluted and in the cleaner areas, averaged over one year, were 2.7 and 1.3 respectively. Since the pollution in this area was due to a single large source, pollutant levels fluctuated widely. One peak reading of over 35 mg/m^3 (13 ppm) was observed, and daily averages ranged up to 17 times the annual mean. Chronic bronchitis rates for men over 55 were higher in the polluted area, but rate differences for other age groups and for women were not statistically significant between the areas. A higher incidence in the polluted area was also found for a variety of respiratory symptoms such as head colds, wheezing, and chronic cough. The effects were said to have disappeared when pollution was reduced by using a higher stack at a smelter.[54] Adjustments were not made for differences, which were known to exist, in age and smoking between the two areas. In addition, the heavily polluted area was of lower socioeconomic class: only 3.2 percent of its population was in professional and administrative occupations, and 10.2 percent were laborers as compared to 10.2 percent professionals and 2.4 percent laborers in the clean area. A difference of over one inch in average height of the population in the two areas also indicates that the two populations were not completely comparable. No significant differences that could be related to air pollution were found in respiratory function measured as $FEV_{1.0}$. In Port Kembla, SO_2 concentrations are highest during the summer, rather than winter, so that this study is not biased by the question of whether the effects are due to pollution or low temperature, as has been the case in many of the British and American epidemiologic studies. Notwithstanding the stated deficiencies of the study, the finding that respiratory symptoms disappeared when pollution was reduced would appear to confirm an effect of sulfur dioxide at the level found originally in the old high pollution area of Port Kembla, if no other change took place which could account for the reduction.

In 1965, Holland et al.[55,56] reported on their study of the prevalence of chronic respiratory disease symptoms and performance of pulmonary function tests of outdoor telephone workmen in London, in rural England, and on the east and west coasts of the United States. Types of occupational exposure, use of cigarettes, and socioeconomic matching were considered. The annual mean concentration of suspended particualte matter in the British exposures, both rural and in London, was approximately 200 μg/m^3. For sulfur dioxide, the mean concentrations were: 0.285 mg/m^3 (0.1 ppm) in London and 55 μg/m^3 (0.02 ppm) in rural areas of England. Persistent cough and phlegm and chest illness episodes were 1.4 times as frequent in men aged 40 to 49, and 2.2 times as frequent in men aged 50 to 59, in the London area as in rural England. Increased sputum volume was more frequent and pulmonary function was poorer in London than in the rural areas. These differences held, even when the data were standardized for smoking.

In an earlier study, conducted in 1960 and 1961 following a number of related studies yielding consistent results, Holland and Reid[57] reviewed respiratory symptoms, sputum production, and lung function levels in mail van drivers and vehicle maintenance men in central London and mail van drivers and engineering workers also driving vans in and around three county towns in southern England. The conduct of the study was exemplary. A standardized questionnaire was used as were trained interviewers. Because of the design of the study, socioeconomic factors were the same, the occupational exposures were homogeneous, and corrections were applied for smoking. There were some physique differences in the rural areas, and allowances were made for these in the statistical evaluation. Unfortunately, no comprehensive indices of air polution were available for the three towns. However, mean sulfur dioxide readings expressed as sulfate per 100 cm^2 lead oxide were available for two stations in St. Pancras near the London survey center and two stations in Gloucester, one of the three towns. Brasser et al.[7] have furnished the following SO_2 values: London (St. Pancras) summer average 100 $\mu g/m^3$ (0.035 ppm), winter average 500 $\mu g/m^3$ (0.17 ppm) and Gloucester, Peterborough and Norwich 75 $\mu g/m^3$ (0.026 ppm) and 200 $\mu g/m^3$ (0.070 ppm) respectively for summer and winter averages.

Between the ages of 50 and 59, the London men had more frequent and more severe respiratory symptoms, produced more sputum, and had significantly poorer performance on lung function tests. Dyspnea of grade 3* or more was more than four times as frequent in London as in the county towns among men 50 to 59 years of age; this is a highly significant difference. The authors concluded that the relatively high level of pollution in London was the major reason for the excessive frequency or severity of chronic bronchitis in London.

In a group of Canadian veterans studies by Bates,[58] a relationship between air pollution and both bronchitis and pulmonary function measurements has been reported. There are, unfortunately, inadequate data on the levels of smoke, sulfur dioxide, and other pollutants, in the four Canadian cities compared, to derive specific relationships between the levels of these pollutants and the prevalence or exacerbation of disease or the deterioration of pulmonary function. However, there is an association in the "dirty" cities (Montreal and Toronto) versus the "clean" cities (Halifax and Winnipeg) of increased prevalence and severity of bronchitis, and poorer pulmonary function performance.

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*The authors grade dyspnea[56] according to five levels; grade 3 represents dyspnea when walking even at a slow pace on level ground, but not to the extent that it is necessary to stop for breath.

One of the most detailed and carefully designed American studies was carried out in Berlin, New Hampshire, and Chilliwack, British Columbia.[59-61] In each town a carefully drawn, random sample of the population was given standard pulmonary function tests and a standard questionnaire for respiratory symptoms. In Berlin, the sulfation rate for August and September 1960 averaged 426.0 $\mu g/100\ cm^2$-day while in Chilliwack the sulfation concentration for August and September 1963 averaged 50.3 $\mu g/100\ cm^2$-day. This was converted to an equivalent sulfur dioxide value for Berlin of 35 $\mu g/m^3$ (0.012 ppm) based on readings for one station. No information is provided to show how the Chilliwack sulfation values were converted to an SO_2 equivalent of 2.85 $\mu g/m^3$ (0.001 ppm). Soiling values were virtually identical; coh values averaged 0.5 for Berlin and greater than 0.5 for Chilliwack. The prevalence of chronic respiratory disease was initially greater in Berlin, but adjustments for differences in age and in cigarette smoking eliminated all the differences in prevalence. However, even after correction for age, height, sex, and smoking habits, the Berlin residents had slightly lower results on pulmonary function tests ($FEV_{1.0}$ and Peak Expiratory Flow Rate). This difference might be due to the different climates, or to a slightly lower socioeconomic class in Berlin, or to ethnic differences between the two towns, or to occupational exposures. There were also studies comparing areas within Berlin, and no difference in respiratory symptoms or pulmonary function could be found between an area where the sulfation rate averaged 610 $\mu g/100\ cm^2$-day (2-month period) and another area of the town averaging 255 $\mu g/100\ cm^2$-day for the same period.[59,60,62] As in the two-town study, the disease rates in the two areas of the town were strongly affected by differences in the proportions of the populations who were cigarette smokers. The authors correctly note the limited possibility of ascertaining effects, due to the very low pollution values and the movement of people with respiratory disease to the even less polluted areas of Berlin.

A study[63] comparing two areas exposed to pollution from a single source was undertaken in the Seward-New Florence area of Pennsylvania. The sulfation rate was 6.2 times greater in Seward (3.7 mg SO_3/100 cm^2-day) than in neighboring New Florence, while suspended particulate matter concentrations were 1.4 times greater. These were 151 and 109 $\mu g/m^3$ respectively. During the study period from October 1959 to April 1960, the average 24-hour SO_2 measurement was 255 $\mu g/m^3$ (0.09 ppm) in Seward, compared to less than 30 $\mu g/m^3$ (0.01 ppm) in New Florence, both by the West-Gaeke method. Slightly higher values for airway resistance were found in Seward even after correcting for differences in height and age. No adjustment was made for other factors which may have affected airway resistance, such as smoking and occupation. The difference in body height is also difficult to interpret.

The Nashville air pollution study reviewed total morbidity in relation to air pollution.[47] The morbidity data were obtained by trained interviewers in a questionnaire survey of sample households in the city. The aerometric data used for the survey were the same as those used for the morbidity study. An area of "high" SO_2 concentration was defined as one which had a geometric mean annual 24-hour level of 30 $\mu g/m^3$ (0.01 ppm) or more. The "low" SO_2 area had 15 $\mu g/m^3$ (0.005 ppm) or less. The high sulfation area had 0.351 mg SO_3/100 cm^2-day or more as an annual geometric mean. Areas of high, moderate, and low pollution were also defined by soiling index, annual dustfall, and suspended particulate matter. As expected, when the data were analyzed by socioeconomic class, higher illness rates were reported from the lower class households, and there was a strong tendency for persons of lower social class to be resident in areas of high air pollution.

Since only persons of the large middle class were present in all pollution zones, analyses controlled for socioeconomic status were limited to it. A direct correlation between illness rates from all causes and pollution could not be shown with any consistency except for persons 55 years and older (both sexes). A decline in morbidity rates from high to low pollution areas could be shown for this group with the soiling index and SO_2 concentrations as pollutant variables, but no consistent decline with sulfation, dustfall, or suspended particle concentrations was seen. There was no correlation between pollution indices and morbidity rates for cancer, respiratory, or gastrointestinal diseases. Attempts were made to minimize the effect of occupational exposure by studying females keeping house. In this group, a small but consistent gradient in illness from all causes correlated with air pollution indices. No consistent findings could be found for working females from all social classes combined. Because of the possible wide variations within the large group called "middle class," the study may not have taken socioeconomic status wholly into account. The lack of information on cigarette smoking is another deficiency. The morbidity differences that are shown are most striking between the "high" pollution group versus the "moderate" and "low."

d. Morbidity--Incapacity for Work

Dohan[64] and Dohan and Taylor[65] compared respiratory morbidity in hourly employees in five United States cities by use of insurance and personnel statistics of a large electronics company. Hourly employees received insurance payments after the seventh day of illness, provided that a physician's certificate was received. For the 3 study years, the respiratory absentee rates showed a direct relationship to suspended particulate sulfates. The latter concentrations ranged from a low of 7 μg/m^3 in Cincinnati to about 14 μg/m^3 in Camden and Woodbridge, New Jersey, and in Indianapolis, to a high of 20 μg/m^3 in Harrison, New Jersey. A breakdown by type of respiratory disease showed miscellaneous respiratory infections, influenza, and bronchitis to be most directly related to the sulfate levels (see Figure 8-4). Pneumonia, asthma, and sinus disease

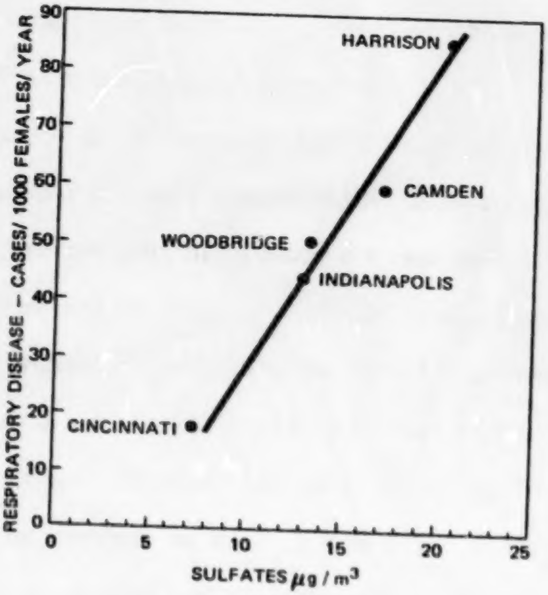

Figure 8-4. Incidence of respiratory disease lasting more than seven days in women versus concentration of sulfates in the city air at test sites.[65] (The incidence of respiratory disease lasting more than seven days in this group is directly related to concentrations of suspended sulfates in the cities shown.)

were not significantly correlated. The incidences of gynecologic problems, urinary tract disease, and appendicitis were not related to several indices of air pollution, including sulfate; nonoccupational accidents did, however, increase progressively with sulfate, as did the respiratory diseases. In addition, neuropsychiatric diseases were highest in the three cities with highest pollution indices. The correlation between all indices of air pollution and accidents and mental illness may indicate that secondary effects of air pollution, such as reduced visibility and gloomy weather, have a measurable effect on health and welfare, or that the results are too nonspecific to attach causal significance.

Age differences were rather marked among the cities, yet age standardized rates were not calculated. Without detailed calculations it is not possible to state whether differences such as only 0.2 percent of the Cincinnati women being over age 45 compared to 35 percent of Camden, New Jersey, women would significantly affect the rates. Differences in social class and standard of living were probably not great, since all subjects were hourly employees of the same company. Differences in patterns of illness reporting and acceptability of different diagnoses within each city are difficult to assess, but presumably were minimized by limiting the study to absences of 8 days and more. Other possible differences, such as weather and climate in the cities, exposure to toxic materials, plant morale, and air conditioning were discussed by the authors and judged by them not to be of major importance. No data are available on differences in cigarette smoking, or plant rules regarding smoking at work, in the different locations. A unique and strong factor of this study is that other pollutants such as total suspended particulate matter, benzene-soluble organics, and certain trace metal concentrations did not correlate with the respiratory disease rates. The findings of this study need to be confirmed.

During 1961-1962 a study of the incidence of incapacity for work was conducted by the British Ministry of Pensions and National Insurance.[66] The population covered was representative of the working population of England and Wales. Rates of sickness absence for bronchitis, influenza, arthritis, and rheumatism were related to indices of pollution. There was a significant correlation between bronchitis incapacity in middle-aged men (35 to 54) and the average seasonal (October through March) levels of smoke and sulfur dioxide in high-density residential districts, based on 24-hour measurements. For Greater London, there was a significant correlation between bronchitis incapacity and both smoke and sulfur dioxide for all age groups taken together, and for men aged 35 to 54 and 55 to 59. It is interesting that there was also more incapacity from arthritis and rheumatism in areas having heavy smoke pollution. Influenza incapacity was greater in those areas with higher pollution levels over Great Britain as a whole but not within the Greater London conurbation, nor was there in this latter area any association between pollution and psychosis or psychoneurosis. The lowest bronchitis inception rates related to smoke levels between 100 and 200 $\mu g/m^3$ and to sulfur dioxide concentrations between 150 and 250 $\mu g/m^3$ (0.053 and 0.081 ppm). The highest values related to concentrations of 400 $\mu g/m^3$ smoke and 0.4 mg/m^3 (0.14 ppm) sulfur dioxide.

In a report by the Committee of the Royal College of Physicians of

London,[67] a study was cited in which it was found that rates of absence of factory and office workers in London began to rise when 24-hour averages of 200 $\mu g/m^3$ of smoke or 250 $\mu g/m^3$ of SO_2 were reached. Temperature changes were found to have no additional effect.

Burn and Pemberton[41] compared areas of high and low pollution in Salford, England. Pollution data were obtained from five standard D.S.I.R. instruments operating for 2 years, 1958 and 1959. The aerometric data were obtained for 24-hour periods. Average daily sulfur dioxide concentrations during the winter months in the more polluted areas were approximately 0.715 mg/m^3 (0.25 ppm) compared to 0.285 mg/m^3 (0.10 ppm) in the cleaner areas (measurement method not clear). Smoke pollution was also considerably higher in the polluted areas. Bronchitis morbidity, as measured by incapacity certificates from the Ministry of National Insurance, was higher for the study group (men aged 45 to 64) in the polluted areas.

Brasser et al.[7] have reanalyzed the Salford data without indicating why this reanalysis was necessary. They prepared new isopleths and concluded that the correlations between absenteeism for bronchitis and pollution levels are considerably higher than originally presumed by the investigators themselves. The population 45 to 64 used for denominators of the rates had to be estimated by assuming that each district had the same proportion in that age group as the town as a whole. In addition, large differences in socioeconomic class probably existed between the areas, but no adjustments were possible. Differences in occupation may also have affected incapacity rates. No data on cigarette smoking were available.

Results obtained in The Netherlands have also shown that when the

SO_2 concentration rose for 3 to 4 days from about 0.30 to 0.50 mg/m^3 (0.11 to 0.19 ppm), absenteeism at both Rotterdam and Vlaardingen increased by at least 30 percent; in certain groups (e.g., those over 45 years of age) the increase was as large as 50 to 100 percent.[7]

Belanger[68] made a study of the effects of air pollution on respiratory hospital admissions in Philadelphia for the year 1966. There was very strong correspondence between soiling index and total respiratory admissions. An additional weak relationship between SO_2 and total respiratory admissions was also noted. He concluded that soiling index is definitely preferred over suspended dust or SO_2 as a measure of potential health effects.

Verma et al.[69] presented information on illness absences in relation to air pollution. Illness data for the employees (males and females, ages 16 through 64) of a metropolitan New York insurance company were obtained through the records of the personnel department. They included medical history, X-ray information, and laboratory results obtained by the medical department of the company, and were classified by absences due to respiratory illness and to nonrespiratory illness. Mean daily concentrations of air pollutants and meteorologic data were secured from the monitoring system of metropolitan New York: smoke shade, sulfur dioxide, and carbon monoxide content were reported. The data for the 2 years, 1965 and 1966, were examined statistically and several conclusions were reached. There was a strong time dependence and a yearly cyclical behavior; when these factors were removed there remained no strong positive relationship between respiratory absence and the pollution variables studied. Respiratory illness absence rates were at their highest level when sulfur dioxide and smoke shade levels were both high on cool days; a lag effect for respiratory absences was not noted.

3. Studies of Children

Comparisons of the prevalence of respiratory disease in areas of varying pollution levels have been made to delineate the roll of air pollution and specific pollutants. A problem common to all the studies is the difficulty in guaranteeing that the areas are similar (except for air pollution) in all factors that might affect the prevalence of disease.

Because studies on adults tend to be complicated by smoking habits, changes of occupation, and changes in address over a period of years, several studies have been directed at effects of air pollution on school children. The advantages of using children for research on the primary etiologic effects of air pollution was first noted several years ago;[70] Anderson has most recently reaffirmed this view.[50] A major element of concern is that deleterious effects on the respiratory system of very young children may have an effect on the subsequent evolution of the chronic bronchitis syndrone in the adult population.

The relationships of respiratory infections in children to long-term residence in specific localities have been studied in England by Douglas and Waller.[71] Levels of air pollution, in terms of domestic coal consumption records, were used to classify four groups; the authors include an evaluation of the validity of this method at the end of their report. The histories of 3,866 children born during the first week of March 1946 were followed until 1961, when the children were 15 years of age. Social class composition of these children did not differ significantly from area to area. Measured concentrations for smoke and for SO_2 in 1962 and 1963 were compared with the earlier prediction of pollution intensity based on the coal consumption data, and indicated an overlap for greater London area of low and moderate groupings; for other areas, the predicted gradient of concentrations was affirmed. Sulfur dioxide varied from about 90 $\mu g/m^3$(0.031 ppm) in the "very low" group to about 250 $\mu g/m^3$(0.087 ppm) in the "high" pollution group. Because of the age of the subjects, smoking was apparently not considered in this evaluation. In 1965, 19 percent of the boys and 5 percent of the girls, aged 11 to 13, smoked at least one cigarette a week regularly.[72]

In the Douglas and Waller study, the generation of pollutants in the indoor home environment (e.g., by heating and cooking) was not considered. Interviews were conducted with the mothers when the children were 2 and 4 years of age; information was obtained about upper and lower respiratory illness and recorded hospital admissions for these and other causes. Data about colds, coughs, and hospital admissions were also gathered by school doctors at medical examinations when the children were 6, 7, 11 and 15 years of age. Between the ages of 6-1/2 and 10-1/2, special records for causes of school absence exceeding one week were reviewed with the mothers. Families numbering 3,131 remained in the same pollution area throughout the first 11 years of this study. The conclusions of the study were that upper respiratory tract infections were not related to the amount of air pollution, but that lower respiratory tract infections were. Frequency and severity of lower respiratory tract infections increased with the amount of air pollution exposure, affecting both boys and girls, and with no differences detectable between children of middle class and working class families. This association was found at each of the examination ages, including age 15. At age 15, persistence of rales and rhonchi (chest noise), possibly the prodrome of adult chronic respiratory disease, was some 10-fold less in the very low pollution area, and a factor of 2 less in the low pollution area than that in the high pollution area. If the 1962-1963 measured concentrations for smoke and SO_2 can truly be extrapolated to the 15-year respiratory illness survey, then these British school children experienced increased frequency and severity of lower respiratory diseases in association with annual mean smoke concentrations ranging above 130 $\mu g/m^3$ and SO_2 above 130 $\mu g/m^3$ (0.046 ppm).

The lower respiratory tract findings of Douglas and Waller were confirmed in a study by Lunn et al.[73] The patterns of respiratory illness in school children of the age group 5 to 6 were studied by them with reference to residence in four areas of Sheffield. The data were collected during the summers of 1963, 1964, and 1965 in order to minimize effects of winter respiratory illness upon the pulmonary function tests. Mean daily smoke levels measured in each of four areas ranged from 97 $\mu g/m^3$ in the "low" area to 301 $\mu g/m^3$ in the "high" area. SO_2 concentrations were respectively 0.12 mg/m^3(0.043 ppm), 0.18 mg/m^3 (0.063 ppm), 0.22 mg/m^3(0.077 ppm), and 0.28 mg/m^3(0.10 ppm) in the four areas, during 1963-1964. Somewhat lower smoke levels were noted the following year, although the gradient between the districts was preserved. However, the sulfur dioxide values were obtained at five schools between October 1965 and May 1966 inclusive. The values were 0.11 mg/m^3(0.038 ppm) and 0.13 mg/m^3(0.047 ppm) corresponding to the "low" pollution area, and then 0.19 mg/m^3(0.068 ppm), 0.241 mg/m^3

(0.085 ppm), and 0.304 mg/m^3 (0.11 ppm) respectively. Questionnaire of the parents, physical examination, observation for the presence of nasal discharge, examination of the eardrums, and recording of both the forced expiratory volume in 0.75 seconds ($FEV_{0.75}$) and the forced vital capacity (FVC), were completed during each of the summer terms of 1963, 1964, and 1965. Several socioeconomic factors were compared for the various districts; smoking was appropriately disregarded for this age group; internal home environments, or differences in home heating systems, were not reported. The authors conclude that there is an association between the levels of atmsopheric pollution and chronic upper respiratory infections (as indicated by mucopurulent nasal discharge, history of three or more colds yearly, or scarred or perforated eardrum). Further, lower respiratory tract illness (measured by history of frequent chest colds or episodes of bronchities or pneumonia) was similarly associated. Functional changes, in the form of reduced $FEV_{0.75}$ ratios, emerged where there was a past history of pneumonia or bronchitis, of persistent or frequent coughs, or of colds going to the chest. There appeared, therefore, to be a persistence of respiratory dysfunction, even in the absence of high pollution extant at the time of the function testing. This study clearly demonstrated the association between respiratory illness in infant school children and atmospheric pollution. The lowest "effect" level for smoke and SO_2 was not clearly indicated by this study, but the increased association of "respiratory infections" in school children was detected in areas whose mean daily figures exceeded about 100 μg/m^3 for smoke and 0.12 mg/m^3(0.042 ppm) for SO_2.

Lunn et al.[74] conducted a followup study of Sheffield School children. Additional findings were reported on two groups: first, a group of 11-year old children attending the same schools as the 5-year olds and examined at the same time in 1963, 1964, and 1965; second, the original group of 5-year olds re-examined four years later in 1967, 1968, and 1969 (when they were nine years old). The data were taken to determine if the 11-year old children showed the same pattern as the 5-year old children in the original sample and whether the contrasts shown by the original sample of 5-year old children had persisted in them several years later. Followup data were obtained on 558 nine-year old children who were first seen and reported on at the age of 5. Data on 1,049 eleven-year olds seen at the same time were also collected. The 11-year olds had a lower prevalence of respiratory illness than the 5-year olds seen at the same time. An excess of respiratory illness found among the 5-year olds living in areas of "high pollution" was also observed in the 11-year olds but to a lesser degree. The original group of 5-year olds seen four years later (at 9-years old), had less respiratory illness than the 11-year old group seen previously and showed no differences of significance between areas. It was noted that these changes can be correlated with the overall improvements in pollution levels in Sheffield and the narrowing contrasts between geographic areas, suggesting that the Sheffield Clean Air Programme has already shown effect.

In another English survey[75] chronic otitis media was found, during examination for National Service, to be higher in youths from towns than those from the country. A comparative study of 600 children at

Sheffield and 400 in a rural district of Wales aged 10-12 years found that perforated eardrums and discharging ears were commoner in the Sheffield children than in the Welsh children of the same social class. Another study in Sheffield found persistent cough and scarred or perforated eardrums were more common in those districts with high pollution. As a part of the National Survey of Health and Development, health visitors and school doctors examined 3,866 children born in 1946. There was little difference in frequency of upper air passage infections, but there was evidence that tonsillitis and discharging ears were less common in rural areas with low pollution. Also repeated infections of the bronchi and lungs in infancy that caused admission to a hospital or absence from infant school were more common in heavily polluted areas.

A study by Manzhenko[76] of upper respiratory tract conditions in school children in Irkutsk is difficult to relate to the Sheffield study. However, the higher incidence of respiratory tract conditions and the undefined abnormal X-ray findings in these children's lungs are disturbing evidence of the possibility of an association between serious respiratory disease and residence in a polluted community.

Paccagnella et al.[77] investigated health effects of air pollution in various sections of Ferrara, Italy on school children over the period 1959 to 1964. First, it was learned that air pollution in Ferrara is not very high when compared with other urban centers. Even so, there were significant differences which occurred mainly in the winter, in the daily average concentrations of suspended particles and SO_2 in residential zones at various locations in the city. They concluded that there was an association between climatic factors, air pollution, and respiratory disease. The effect of climatic factors was found to be greater than the air pollution factors on respiratory disease. It was concluded, however, that the partial correlation between air pollution and respiratory disease was significant.

Toyama[52] studied two groups of school children, 10 to 11 years old, in Kawasaki, Japan. Sulfation rates at the school in the more polluted area varied from 0.5 to 1.9 and averaged 0.9 mg/100 cm^2-day PbO_2; no sulfation rates were given for the area of lower pollution. The children from the more polluted area had a higher frequency of nonproductive cough, irritation of the upper respiratory tract, and increased mucus secretion. The dustfall rate was considerably lower in the less polluted area except for an occasional month when the dustfall in the two areas was almost equal. Whether the effect was due to oxides of sulfur or particulate matter cannot be determined from this study.

4. Studies of Pulmonary Function

Spicer et al.[78] studied a group of patients with chronic obstructive airway disease who resided in a small area of downtown Baltimore. Air samplers were placed at the residential area and at the University, where extensive pulmonary function tests were performed. The patients became better or worse in their pulmonary function as a group, suggesting that they were influenced by a factor in their common environment. It was not, however, possible to determine a simple cause and effect relationship with any one pollutant. Subtle changes in the pollutant concentrations and weather conditions may have been responsible.

Shephard et al.[79] studied a group of 10 cardiac cripples who were confined to their homes. Air pollution measurements were carried out by sampling equipment placed inside the homes. Pulmonary function tests were repeated at the same hour of the day, 3 times weekly, for 2 months. Although a response to suspended particulate pollution was demonstrated, no consistent changes in pulmonary function were noted with sulfur dioxide levels, measured as total gaseous acid (sic). During one inversion period, a 6-hour average of sulfur dioxide concentrations (hydrogen peroxide titremetric method) reached 0.460 mg/m^3(0.16 ppm). The indoor readings were considerably lower, the highest indoor concentration being sustained for 6 hours.

Holland et al.[56] report decreased performance of the $FEV_{1.0}$ test in London and British rural outside telephone workers compared with their American counterparts. For both groups the FEV was further decreased in relation to smoking intensity. FEV differences within the United Kingdom workers (i.e., London versus rural), may be related to an appreciable extent to the sulfur dioxide concentrations accompanying the particulate levels. A more detailed discussion of the study appears in Section C-2-c.

Toyama[52] reported measurements of peak flow rate and total vital capacity performance in Japanese school children in areas of differing air pollution measured monthly; fluctuations were observed in the mean peak flow rates of children attending schools and living in polluted industrial areas, and the variations were smaller for children in cleaner areas. Total vital capacity was not significantly different among pupils of the various schools. There was a substantial difference in peak flow rates between the two school districts at times of highest pollution. When pollution values were lowest, the differences were less. Monthly dustfall was 15 to 70 tons/km^2-mo in the more polluted areas; lead peroxide candle sulfation rates from month to month ranged from 0.5 to 2 mg SO_3/100 cm^2-day in the higher polluted area.

In Osaka, Watanabe[22] studied the peak flow rate and vital capacity performances of children in schools enduring differing air pollutant concentrations. It was noted that individual peak flow rates were more markedly decreased in the winter months (September to December 1963) for the school in the highly polluted area than for the school in the low pollution area. Daily mean concentrations of both dustfall and sulfur dioxide concentrations were twice as great in the polluted area as in the unpolluted area.

In the paper by Lunn et al.[73] Sheffield school children were shown to have reduced $FEV_{0.75}$ and FVC ratios in the area of highest pollution. The measurements were made during the summer, when pollution levels were low and apparent incidence of acute respiratory infection was diminished, suggesting, in contrast to the Japanese studies referred to above, that there may be persistence of the respiratory function deterioration in relation to residence in the area of high pollution. Mean daily averages measured at a single station were: smoke, 300 $\mu g/m^3$; SO_2, 0.27 mg/m^3(0.096 ppm). In the Port Kembla study[53] mentioned in Section C-2-c of this chapter, no significant differences in pulmonary function were noted which could be attributed to air pollution.

The studies relating morbidity and deterioration in pulmonary function to particulate levels cover effects which are also included in Level III of the World Health Organization's "guides to air quality."[25]

5. Studies of Panels of Bronchitic Patients

Lawther and Waller[80,81] related several episodes of acute urban pollution to a worsening of condition in a group of bronchitic patients, well studied in a registry at St. Bartholomew's hospital in London. Changes in their symptomatology were recorded in a daily diary, and acute worsening in significant numbers of the group was associated with daily rises in air pollution above 300 $\mu g/m^3$ of smoke and 0.60 mg/m^3(0.21 ppm) of sulfur dioxide. Figure 8-5 shows graphically the effects observed on 29 bronchitic patients of high pollution levels in January 1954.

Angel et al.[82] reviewed the occurrence of new respiratory symptoms in men working in factories and in offices, most of whom had prior evidence of chronic bronchitis. The study group of 85 men, observed through the winter of 1962-1963, was selected from a group of 1,000 men,

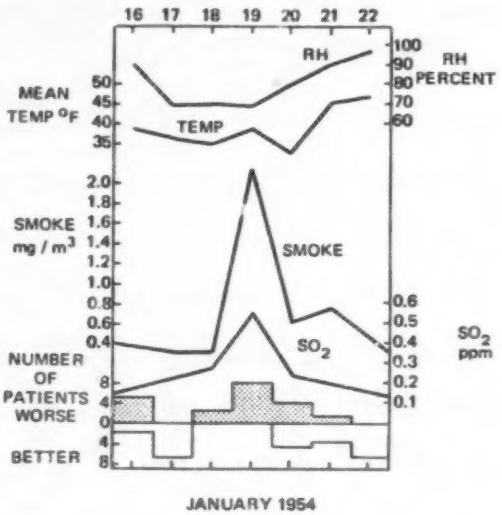

Figure 8-5. Effect on bronchitic patients of high pollution levels (January 1954).[80,81] (This figure represents the effect on bronchitic patients of increased pollution levels; patients stated whether they regarded their condition as "worse" or "better".)

aged 30 through 59, without apparent classification of either smoking patterns or possible occupational or residential exposure differences. Increased sputum production, deterioration of pulmonary function performance ($FEV_{1.0}$), and the more frequent occurrence of respiratory symptoms classified as "upper" (coryza, influenza, and acute respiratory disease), and "lower" (chest colds, bronchitis, wheezy attacks, pneumonia), were all associated with increases in both smoke and sulfur dioxide concentrations. There was frequently difficulty in defining an exacerbation of disease in those individuals already experiencing chronic bronchitis. During this period, illness peaks (attack rate) may have occurred with weekly mean concentrations of smoke exceeding 400 $\mu g/m^3$ and of sulfur dioxide exceeding 0.46 mg/m^3(0.16 ppm); weekly mean concentrations were calculated using the highest daily mean occurring each week at each of 13 locations in the area.

Carnow et al.[83] studied over 500 patients with respiratory disease in Chicago during the winter of 1966-1967. Semidaily averages of sulfur dioxide (West-Gaeke Method) were computed from eight continuous monitoring stations in Chicago for the hours of 6 a.m. to 6 p.m., and for 6 p.m. to 6 a.m. Pollution by particulate matter was also present but not analyzed in this report; the geometric mean for particulate in Chicago during 1964-1965 was 148 $\mu g/m^3$, according to the National Air Surveillance Network (NASN) data.[84] The semidaily averages were used to estimate the 24-hour average concentrations of sulfur dioxide to which the patient was exposed at work and at home. The chronic bronchitics were divided into two groups according to the severity of their disease, and the analyses were kept separate for the two groups.

For patients aged 55 and over with severe bronchitis, a significant association was demonstrable between the level of sulfur dioxide and person-days of illness. The differences in illness rates in this group for different levels of exposure was most marked for disease on the day following exposure. A marked rise in illness rate was noted for patients exposed to 0.71 mg/m^3(0.25 ppm) of sulfur dioxide or more. (See Figure 8-6.)

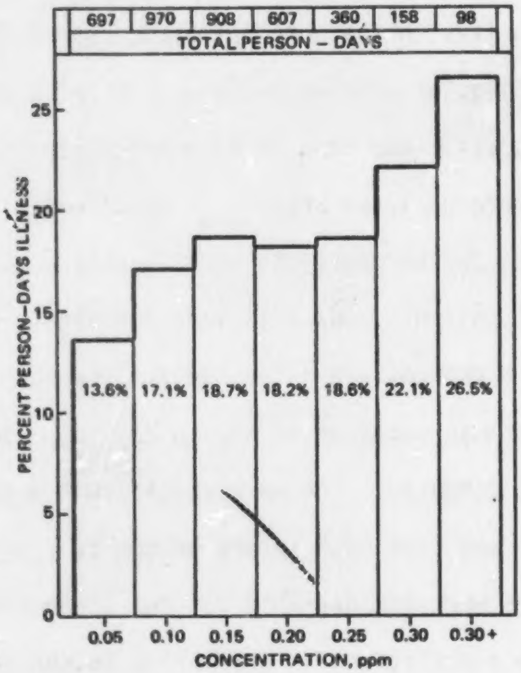

Figure 8-6. Comparison of person-days of acute illness with seven levels of sulfur dioxide exposure in Chicago, in patients with severe chronic bronchitis (age 55 or more), for October-November 1967. (There is an increase in illness for bronchitics over age 55 with increase in sulfur dioxide concentrations; the relationship is with 24-hour SO_2 levels on the day prior to illness.)

For patients under 55, no differences in illness were noted with exposure, except for the group exposed to 0.86 mg/m^3(0.30 ppm) or more of sulfur dioxide.

For the patients with mild bronchitis, illness was not related to air pollution in those aged 55 and over, while those under age 55 seem to be worse when exposed to more than 0.86 mg/m^3(0.30 ppm) SO_2. These analyses indicate that groups of persons exposed to higher levels of sulfur dioxide tend to experience higher rates of acute respiratory diseases. However, the group with higher respiratory illness rates could merely happen to live in the more polluted areas. The situation is similar to the findings of most epidemiologic studies which indicate that persons of low social class tend to have high illness rates and also tend to live in more polluted areas. In an attempt to eliminate this class-site factor, further analyses were therefore carried out for the same groups of patients, but this time for single months, using each patient as a control against himself. For each patient, the difference between his mean exposure to SO_2 on days of illness and on days of no illness was computed. The only significant differences were for those aged 55 and over with severe bronchitis; no statistically significant differences were demonstrable for the other groups. This tends to show that the association for bronchitis in the younger age group mentioned above was more likely due to another factor.

An association between sulfur dioxide concentration and illness ratio in only one age group could be regarded as a chance happening. Yet the elderly patient with severe chronic bronchitis would appear to be especially susceptible, since this group is also heavily involved in the excess deaths of acute pollution episodes in London and New York. Accordingly, it seems reasonable to infer, as the authors did, that there is in all likelihood an effect of high daily levels of sulfur dioxide on older patients with advanced bronchitis; this effect is one of precipitating illness and of exacerbating symptoms. The technique used in this study of developing a personal pollution index estimated for each patient with regard to his place of employment and residence adds confidence to the authors' analysis.

An increase in respiratory symptoms was noted among elderly emphysematous individuals in a rest home in the Ruhr area during December 9-13, 1959. The complaints included breathlessness, throat and eye irritation, and depression and apathy (without further specification). The estimated mean indoor sulfur dioxide concentration was 0.54 mg/m^3(0.20 ppm) for 24 hours. Although the method of measurement was not specified, it probably was the Woesthoff method. For the same period, at an estimated 24-hour indoor sulfur dioxide concentration of 0.27 mg/m^3(0.10 ppm) for 4 days, there was an increase in functional disturbance.[7,8,85]

Patients with preexisting chronic respiratory disease in general seem to have an exacerbation of their symptoms when the sulfur dioxide level exceeds 0.60 mg/m^3 (approximately 0.2 ppm) for 24 hours or more in the presence of a substantial amount of unmeasured particulate pollution.

Ishizaki et al.[86] studied respiratory symptoms of a group of subjects with chronic bronchitis in connection with the Tokyo-Yokohama area. Approximately 1,000 male workers in a casting company were questioned about respiratory symptoms and 100 were diagnosed as having chronic bronchitis for at least three years. Sixty-three men cooperated in the study. Utilizing a daily symptom survey, falling dust, suspended particles, SO_2 concentration, and mean wind velocity were found to be related to the increase and decrease of respiratory symptoms.

In an English summary[87] the effects of air pollution and sudden weather changes on patients with bronchitis was noted by bronchitis patients. Symptoms increased with increased smoke and SO_2 and were less closely related to falls in temperature or changes in humidity. The summary also concluded that, indeed, whatever the pollution index employed, all investigations in Britain have so far shown a close correlation between presumptive pollution level and mortality from bronchitis in middle life. In one survey carried out by the Ministry of Social Security in 1961-1962, the rate of disability attributed to bronchitis was strongly correlated with local levels of SO_2 and, to a lesser extent, of smoke in the places where the men worked.

6. Miscellaneous Studies

Although the major action of sulfur oxides has been assumed to be by surface contact on the mucous membranes of the respiratory system, the possibility of effects on the total body system (systemic effects) must be considered. Sulfur dioxide is absorbed into the blood stream and may produce subtle effects on other organs. A few of the studies mentioned previously have suggested that sulfur oxides are a cause of several kinds of illness, rather than respiratory illnesses alone. Even if it is assumed that sulfur oxides are a cause of these results, the effect observed may be secondary to respiratory tract irritation, or indeed, to errors in diagnostic classifications.

Reports from Czechoslovakia[88,89] suggest that sulfur oxides may have an influence on blood formation in children. However, no details or supporting data for their conclusions are given.

Elfimova and his coworkers[90,91] compared "biochemical blood tests" in areas enduring an average of 2 mg/m^3(0.70 ppm) SO_2 with an area having an average of 0.83 mg/m^3(0.29 ppm). Sulfur dioxide could be detected in a much larger proportion of blood samples from subjects in the polluted districts than in those from subjects in the clean district. Ascorbic acid levels were also measured and presumably were lower in the polluted area, but the two published versions seem to have conflicting values. At best, these studies indicate a need for further research, probably in the laboratory, and are not yet sufficiently described to warrant their utilization in air quality criteria.

Yanysheva[92] found an excess of respiratory disease, anemia, and rickets among Russian children living in a highly polluted area (13.3 to 33.0 mg/m^3, or 4.6 to 11.5 ppm) compared to a control area. Epidemiologic methods and bias factors such as social class are not well described, although the types of anemia reported are the same as mentioned above. Sulfur dioxide levels in these three studies are extremely high even in the "clean" areas, and possibly some error has been made in reporting (or analysis of SO_2), although Yanysheva describes symptoms of respiratory distrubances and material damage that would, in fact, indicate very high levels.

D. EFFECTS OF INDUSTRIAL EXPOSURE

Studies of workers occupationally exposed to pollutants provide a unique opportunity to isolate the effects of various chemicals. By carefully choosing industrial situations, populations can be found which have been exposed to rather high levels of specific pollutants for a long period of time. An extremely serious disadvantage of this type of study for the preparation of air quality criteria is that the exposed workers are gainfully employed, and lack of disease in them may not indicate safety of the concentrations to a general population which includes the elderly and infirm. Sensitive people are either not selected for employment, or are soon lost to employment.

In conjunction with previously described Berlin, New Hampshire, studies, Ferris et al.[93] compared samples of workers from a pulp mill and from an adjacent paper mill. Air concentrations of sulfur dioxide in areas of the pulp mill averaged from 5.7 to 37.2 mg/m^3 (2 to 13 ppm). Occupational exposure at the paper mill was almost nonexistent, and most of the workers had been at the same job in each of the plants for a number of years. Some of the men in the pulp mill were exposed to chlorine as well as sulfur dioxide, and some only to sulfur dioxide. No significant differences were found in respiratory symptoms or in simple tests of pulmonary function between workers in the two mills, but men working with chlorine had slightly lowered respiratory function compared to those exposed to sulfur dioxide alone. A unique feature of this industrial report is that cigarette smoking was allowed for in the analysis. The working men of both mills had a lower prevalence of respiratory disease than the male population of Berlin, New Hampshire, suggesting that working populations may not be representative of the general population.

Skalpe[94] also compared workers from pulp and paper industries in Norway. Sulfur dioxide concentrations at the pulp mill varied between 5.7 and 103 mg/m^3(2 to 36 ppm). No significant difference in age or smoking habits was found between the groups, but exact comparisons similar to those of Ferris were not made. A significantly higher frequency of cough, expectoration, and shortness of breath on exertion was found in the exposed pulp mill workers, the difference being greater in age groups under 50 years. In these younger workers the maximal expiratory flow rate was also significantly lower, but no difference was found in the older men. The older workers had been employed for a longer time, and possibly those most susceptible had already been eliminated from the working population. Even the younger workers, however, had all been employed for over 1 year.

Anderson[95] compared oil refinery workers in South Persia with similar workers not exposed to sulfur dioxide. Exposure periods ranged from 1 to 19 years, and daily concentrations of sulfur dioxide varied between zero and 71.5 mg/m^3(25 ppm) with occasional figures of 286 mg/m^3(100 ppm) recorded. No differences were found between the two groups in several measures of health, including pulmonary function, chest X-rays, or clinical examination.

Kehoe et al.[96] studied 100 refrigeration plant workers who, for periods of 4 to 12 years, had been exposed to concentrations exceeding 28.6 mg/m^3(10 ppm) of sulfur dioxide. Compared with workers in other areas of the plant where no significant exposure to sulfur dioxide was experienced, the exposed workers were found to have a significantly higher incidence of nasal pharyngitis, alternations in sense of smell and taste, and an increased sensitivity to other irritants. In addition, a higher incidence of shortness of breath, increased fatigue, and abnormal reflexes was found in the exposed groups. The incidence of "colds" was not different between the two groups, but the duration of respiratory illnesses was longer in the exposed group. This study was performed shortly after the limitation of exposures by control measures, and concentrations in prior years may have ranged from 229 to 286 mg/m^3(80 to 100 ppm). The data presented are insufficient to determine whether the severe effects noted were limited to the workers who had been exposed to the higher concentrations of previous years.

Lowe et al.[97] have accomplished an epidemiological study of respiratory symptomatology and lung function among men working at two steel plants in South Wales. Measurements of air pollution were compared with respiratory symptoms and ventilatory capacity for 1049 men who spent most of their working hours in one of 114 defined working areas. Mean SO_2 and mean respirable dust were measured. In addition, the effects of age and smoking were studied. The results of the study failed to reveal any relation between respiratory symptomatology and ventilatory capacity of the men and the mean SO_2 and mean respirable dust to which they were exposed. There was no correlation between respiratory disability and atmospheric SO_2. They conclude that SO_2 is probably not the important component of atmospheric pollution as far as the aetiology of chronic bronchitis is concerned.

Thus the industrial exposures suggest that no significant effect on health or pulmonary function can be noted at exposures up to about 5.7 mg/m^3(2 ppm) for the working hours of the day over a period of several years. In these situations there is a lack of a demonstrable effect of exposure to relatively pure sulfur dioxide at concentrations that are well above those implicated in ambient exposures. However, as noted previously, studies of occupational exposure have severely limited value for the preparation of ambient air quality criteria.

The effects on both morbidity and mortality demonstrated for community exposures are probably a result of the synergism of the sulfur dioxide and the suspended particulates found in the ambient atmosphere rather than the effects of either pollutant alone. The data regarding the industrial exposures are summarized in Table 8-3.

Table 8-3. INDUSTRIAL EXPOSURES

Comparison	Level of Exposure, $\mu g/m^3$ SO_2	Effects	Reference	
			No.	Author
Pulp versus paper mill workers Berlin, New Hampshire	5,700 to 37,000	No difference in pulmonary function or respiratory disease prevalence rates after control for cigarette smoking	93	Ferris *et al.*
Pulp versus paper mill workers Norway	5,700 to 103,000; many over 30,000	Excess cough, sputum, and expectoration under age 50. No effect over age 50.	94	Skalpe
Exposed versus non-exposed oil refinery workers, South Persia	0 to 71,500; over 286,000 occasionally	No effect on pulmonary function, chest X-ray or clinical examination	95	Anderson
Exposed versus non-exposed refrigeration plant workers, United States	over 28,000; 286,000 at times	Increased shortness of breath and fatigue and abnormal reflexes. Longer duration of "colds." No effect on respiratory disease *incidence*.	96	Kehoe *et al.*

E. SUMMARY

This chapter reviews epidemiologic studies of the relationship between pollutant concentrations and their effects on health. Indices varying from disturbance of lung function to death are considered.

In considering levels of pollution at which health effects occur, attention must be given to the averaging time employed in the original observation, because of the typical log-normal distribution of sulfur oxide concentrations, long-term averages are considerably lower than short-term averages in the same locations.

Short-term exposure to sulfur oxides may produce symptoms and illness in otherwise healthy people, but the magnitude of the effects and concentrations necessary to produce the effects are not well defined and exposures are generally substantially higher than the levels cited in the epidemiologic studies.

Over the years, a number of acute air pollution episodes have been reported. Both oxides of sulfur and particulate matter have contributed significantly to the health effects associated with these episodes.

In London, a rise in the daily death rate has been detected when the concentrations of sulfur dioxide rose abruptly to levels at or about 0.715 mg/m^3(0.25 ppm) as measured by the hydrogen peroxide titrimetric method in the presence of smoke at 0.75 mg/m^3. The elderly and patients with heart or lung disease were predominantly affected, but others have also been involved, particularly when pollution reached higher levels. Daily concentrations of sulfur dioxide in excess of 1.5 mg/m^3 (0.52 ppm) for 1 day in conjunction with levels of suspended particles exceeding 2 mg/m^3 have resulted in an increase in the death rate of 20 percent or more over base line levels.

In New York City, sulfur dioxide concentrations of 1.5 mg/m^3 (0.52 ppm) (as measured by the hydrogen peroxide titrimetric method) and suspended particulate matter, measured as a soiling index of 6 cohs or greater, have led to increased mortality.

In Rotterdam, a 24-hour mean concentration of 0.50 mg/m^3 SO_2 (0.19 ppm) (hydrogen peroxide titrimetric method) lasting for 3 to 4 days has led to an increased mortality rate. This observation is especially significant because particulate levels are very low in Rotterdam. Even lower levels of pollution from 0.30 to 0.50 mg/m^3 SO_2 (0.11 to 0.19 ppm) for 24 hours, are thought possibly to increase mortality.

Morbidity rates have been increased in all episodes which have resulted in an increased mortality. Thus, in London, increases in emergency admissions to hospitals, calls to general practitioners, and certified sickness asbsence from work have been noted. In Rotterdam increased hospital admissions for respiratory disease, particularly in older persons, have occurred when SO_2 levels have risen to 0.30 to 0.50 mg/m^3(0.11 to 0.19 ppm) and present for 3 to 4 days; there has also been an increase in absenteeism from work which reached 30 percent for all ages and 50 to 100 percent in persons aged 45 and over.

A survey of emergency clinic visits to major New York City hospitals in November 1953 revealed an increase in visits for upper respiratory infections and cardiac diseases in both children and adults in all of the four hospitals studied. Sulfur dioxide levels ranged between 0.20 and 2.5 mg/m^3(0.07 to 0.86 ppm) during the period from November 12 to 24, and hospital admissions had clearly increased by November 16, at which time concentrations had not yet exceeded 0.72 mg/m^3(0.25 ppm); smoke shade at this time was close to 3 coh units.

The most striking effects have been observed in association with exceptional episodes of air pollution. However, lower and more persistent concentrations are also correlated with mortality and morbidity. British studies have indicated an association of bronchitis death rates with air pollution concentrations that is apparently independent of social class differences, but which also do not specify the role played by sulfur oxides. Instead, these studies treat of a combination of sulfur oxides and particulates. In one major study of Eston, sulfur dioxide values for a year averaged 0.115 mg/m^3(0.040 ppm) in the dirty area and 74 μg/m^3(0.026 ppm) in the cleaner area. Smoke values were 160 and 80 μg/m^3 respectively.

In the United States, the Buffalo study indicated an effect on chronic bronchitis disease mortality for men aged 50 to 59 in the low social classes. This finding of air pollution exerting a special effect on the low social classes appears to be consistent with the British findings.

A study in Genoa, Italy, made use of housewives. One of the groups surveyed included women all 65 or more years of age who were nonsmokers, who had lived for a long period in the same area, and who had no industrial exposure.

There was a finding of increased frequency of cough, sputum, dyspnea, and bronchitis in the moderate-pollution area over the cleanest area. A much sharper difference in frequency between the cleanest and the dirtiest area was found. The cleanest area had an annual mean of 80 $\mu g/m^3$(0.028 ppm) of sulfur dioxide, the mean of the moderately clean area was 105 $\mu g/m^3$(0.037 ppm), and the dirty area averaged 265 $\mu g/m^3$ (0.093 ppm). The measurement of sulfur dioxide was recorded by a technique analogous to the volumetric method of the British.

This study also showed a correlation between the frequency of bronchitis and the annual mean of sulfur dioxide levels for the seven districts of Genoa whereas the correlation between the frequency of bronchitis and suspended matter and dustfall was not statistically significant.

In Berlin, New Hampshire, no effect was observed for long-term exposure in areas with sulfation levels averaging 610 $\mu g/100\ cm^2$-day. The authors recognized that the lack of results may have been influenced by the narrow differences in air quality between the areas compared, and they also noted that there probably had been a selected migration of diseased persons to the less polluted areas, which could have affected the results.

Another morbidity study which included housewives was that conducted in Nashville. This showed a direct correlation between illnesses for all causes for housekeeping white females, 15 to 64 years of age, and sulfur dioxide levels. It also showed that morbidity from cardiovascular disease in the 55 and older age group, for both sexes, was twice as high in the most polluted area as compared with the least. However, cigarette smoking was not taken into account and the adjustment made for socioeconomic status may not have been adequate.

The study of Port Kembla, Australia, had shown differences in respiratory symptoms for areas which had long-term values of 95 μg/m^3 SO_2(0.034 ppm) and 25 μg/m^3(0.009 ppm) measured by absorption in a sulfuric acid solution containing hydrogen peroxide. The study is unusual in that the source of pollution was the single stack of a smelter and daily averages were up to 17 times the annual mean. However, the finding that respiratory symptoms disappeared when pollution was reduced through installation of a higher stack, would appear to confirm an effect of sulfur dioxide at the concentrations originally measured, provided that no other change took place which could account for the disappearance of symptoms.

The study of school children in Great Britain indicated that they experienced increased frequency and severity of respiratory diseases when the long-term levels exceeded about 120 μg/m^3(0.046 ppm) SO_2 and 100 μg/m^3 for smoke.

Several studies have been noted relating daily variations in air pollution with changes in the clinical condition of patients with chronic lung disease. A good deal of information exists on the effects of exposure to moderately elevated levels of SO_2 lasting a day to 3 or 4 days. A daily average level of about 0.60 mg/m^3 of SO_2(0.21 ppm) has caused accentuation of symptoms in persons with chronic respiratory disease on the day following the high SO_2 level if particulate matter at a similar concentration was also present.

This finding by Lawther was also observed by Carnow in Chicago. He too noticed a sharp rise in illness rates on the day following exposure to 0.72 mg/m^3(0.25 ppm) of sulfur dioxide (West-Gaeke method) or more for patients 55 and over with severe bronchitis. Particulate matter was also present in the atmosphere.

The study of an elderly emphysematous population in a rest home in the Ruhr area of Germany demonstrated that complaints including breathlessness, throat and eye irritation, and "depression and apathy without further specification" increased at estimated indoor sulfur dioxide concentrations of 0.54 mg/m^3(0.20 ppm) for 24 hours. There was an increase in functional disturbance at an average daily level of 0.27 mg/m^3(0.10 ppm) for 4 days, again an estimated indoor level, measurement presumably being made by the Woesthoff method.

The analyses of the numerous epidemiological studies discussed clearly indicate an association between air pollution, as measured by particulate matter accompanied by sulfur dioxide, and health effects of varying severity. This association is most firm for the short-term air pollution episodes.

There are probably no communities which do not contain a reservoir of individuals with impaired health who are prime targets for the effects of elevated levels of particulate matter and sulfur oxides. However, to show small changes in deaths associated with coincident higher levels of air pollutants requires extremely large populations. In small cities, these small changes cannot be detected statistically.

The epidemiologic studies concerned with increased mortality also show increased morbidity. Again, increases in morbidity as measured, for example, by increases in hospital admissions or emergency clinic visits, are most easily detected in major urban areas.

It is believed that, for the large urban communities which are routinely exposed to relatively high levels of pollution, sound statistical analysis can detect with confidence the small changes in daily mortality which are associated with functions in pollution concentrations. Unfortunately, only limited analysis has thus far been made, and this has been attempted only in London and in New York.

The association between longer-term community exposures to particulate matter for respiratory disease incidence and prevalence rates is conservatively believed to be intermediate in its reliability. Because of the reenforcing nature of the studies conducted to date, the conclusions to be drawn from this type of study can be characterized as probable.

The association between long-term residence in a polluted area and chronic disease morbidity and mortality is somewhat more conjectural. However, in the absence of other explanations, the findings of increased morbidity and of increased death rates for selected causes, independent of economic status, must still be considered consequential.

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APPENDIXES

APPENDIX A—SYMBOLS

A	the cross sectional area of a particle for light attenuation
A_{ij}	the cross sectional area of an i particle (see i and j, below)
C	the sulfur dioxide concentration (ppm or $\mu g/m^3$) in air or the weight (percent) H_2SO_4 in acid droplets
C_o	the minimum concentration which will damage a particular plant in a given time
E	the particle-scattering ratio
E_{ij}	the scattering ratio of an i particle
K	a constant
L_v	visual range
M_g	geometric mean. For sample values x_1, x_2, . . . x_n, the geometric mean is $\sqrt[n]{x_1, x_2, \ldots x_n}$ or $\left\{\prod_{j=1}^{n} x_j\right\}^{\frac{1}{n}}$
N	the number of particles per unit volume of atmosphere
N_{ij}	the number of ij particles per unit volume
P	probability
S_{35}	the radioactive isotope of sulfur having a mass number 35
a	a constant related to damage to a particular plant species by sulfur dioxide
d	the diameter of a spherical particle
e	Napierian log base (=2.718281)
f	the fraction of pollutant gases replaced per unit time with diluting air

g	the acceleration of gravity, cm/sec^2
i	(subscript) identifies a particle of a given diameter and a given index of refraction
j	identifies a particle of a given refractive index
k	the fraction of SO_2 loss per unit time due to oxidation to SO_3
n	the index of refraction
p	the coefficient for converting L_r to desired units
r	a constant related to the minimum SO_2 concentration that damages a particular species of plant
r	correlation coefficient
t	the exposure time
z	"standard normal exceedance deviate". The number of standard deviations an observed value is from the median when the underlying distribution is normal.
λ	the wavelength of light in Angstroms, microns, or nanometers
ρ	the density of a particle or droplet
σ	the attenuation coefficient per unit path length
σ_g	standard geometric deviation
x	probability function, usually expressed as x^2 ("CHI SQUARE")
Σ	summation, or sum of a series

APPENDIX B—ABBREVIATIONS

Å	Angstrom, $1\ \text{Å} = 10^{-8}$ cm
CAMP	Continuous Air Monitoring Project
coh	coefficient of haze
cm	centimeter, $1\ \text{cm} = 10^{-2}$ m
CMD	count median diameter
cm^2	square centimeter
DSIR	Department of Scientific and Industrial Research (England)
FEV	forced expiratory volume
FVC	forced vital capacity
g	mass, grams
hr	hour
LC_{50}	concentration of toxicant lethal to 50% of subjects
l	volume, liters
MMD	mass median diameter
m	length, meters
m^3	cubic meter
mi	mile
mi^2	square mile
min	minutes
μ	micron, $1\mu = 10^{-4}\ \text{cm} = 10^{-6}$ m
μg	microgram, $1\ \mu\text{g} = 10^{-6}$ g
mg	milligram, $1\ \text{mg} = 10^{-3}$ g
MRC	Medical Research Council
mμ	millimicron, $1\ \text{m}\mu = 10^{-9}\ \text{m} = 1\text{nm}$
NASN	National Air Surveillance Network
nm	nanometer, $1\text{nm} = 10^{-9}\ \text{m} = 1\text{m}\mu$
mo	months
ppb	parts per billion
ppm	parts per million
pphm	parts per hundred million
RH	relative humidity
sec	seconds
yr	year

APPENDIX C--CONVERSION FACTORS

To Convert	*To*	*Multiply By*
mg/m^3	µg/m^3	1000
µg SO$_2$/m^3 (0°C, 760mm Hg)	ppm SO$_2$ (vol)	3.5×10^{-4}
µg SO$_2$/m^3 (0°C, 760mm Hg)	ppm SO$_2$ (wgt)	7.7×10^{-4}
ppm SO$_2$ (vol)	µg SO$_2$/m^3 (0°C, 760mm Hg)	2860
ppm SO$_2$ (wgt)	µg SO$_2$/m^3 (0°C, 760mm Hg)	1290
µm	cm	10^{-4}
Å	cm	10^{-8}
m	ft	3.28
lb	g	453.6
µg	g	10^{-6}

APPENDIX D—GLOSSARY

Abscission—the natural separation of flowers, fruit, and leaves from plants by the development and subsequent disorganization of a separation layer

Aerosol—a cloud of solid particles and/or liquid droplets smaller than 100μ in diameter, suspended in a gas

Airway—any part of the respiratory tract through which air passes during breathing

Airway resistance—resistance to the flow of air in the passages to the lungs

*Ala (*pl. *alae) nasi*—the outer part of the nostril

Alpha rhythm—a uniform set of electroencephalographic waves with a frequency of approximately ten per second

Alveolus (pl. alveoli)—a small, sac-like dilation at the inner most end of the airway, through whose walls gaseous exchange takes place

Anemia—a condition in which the number of red blood cells per cubic centimeter of blood is below normal; can be further characterized by descriptions of the alterations in the red blood cells (e.g., *hypochromic, microcytic*) or of the clinical state it is associated with

Anhydride—a chemical compound derived by the extraction of a molecule of water from the original molecule

Anoxia—a deficiency of the amount of oxygen reaching the body tissues

Arrest, cardiac—the cessation of heartbeat

Atelectasis—the collapse of all or part of a lung, with resultant loss of functioning tissue

Atropine—a parasympatholytic drug which in general tends to relax smooth muscle, slow the heart rate, and dilate the pupils

Attenuation—in physics, any process in which the flux density (or power, amplitude, intensity, illuminance, etc.) of a "parallel beam" of energy decreases with increasing distance from the energy source. A more general usage of this word is also found in this publication: any reduction in strength, density, effect, or amplitude.

Auscultation (adj. *auscultatory*)—the act of listening for sounds within the body, usually with the use of a stethoscope

Bloom, crystalline—the formation of very small crystals on the surface of organic films, resulting in noticeable bloom caused by the efficient scattering of light

Bradycardia—an abnormal slowness of the heartbeat

Bronchiectasis—a chronic dilatation of a bronchial passage

Bronchiole—one of the finer subdivisions of the bronchial tree

Bronchitis—an inflammation of the bronchi, usually manifested clinically by cough and the production of sputum

Bronchitis, chronic—a long-standing inflammation of the bronchi characterized by excessive mucus secretion in the bronchial tree and manifested by a persistent or recurrent productive cough. For the purposes of definition, these symptoms must be present on *most days* for a minimum of *3 months* of the year for at least *2* successive *years* (American Thoracic Society)

Bronchoconstriction—a diminution in the size of the lumen of a bronchus

Bronchodilatation—an increase in the size of the lumen of a bronchus

Bronchus (pl. *bronchi*)—one of the larger air passages in the lung

Buffer—a substance capable of enabling a system to resist changes in condition; a solution whose pH is changed only slightly by the addition, within limits, of an acid or a base

Cannula—a small tube for insertion into a body cavity or into a duct or vessel

Capacity, forced vital (FVC)—the largest amount of gas which can be forcibly expired from the lungs following a maximal inspiration

Capacity, functional residual (FRC)—the volume of gas remaining in the lungs as the resting end-expiratory level

Capacity, vital—the maximum volume of gas which can be expired from the lungs following a maximum inspiration

Carcinogenesis—the production of cancer

Carina—a ridgelike structure; in anatomy of the respiratory tract, it is a prominence on the lowest tracheal cartilage and is situated between the orifices of the two mainstem bronchi

Catalyst (adj. *catalytic*)—a substance capable of increasing the velocity of a reaction without chemically or physically changing itself

Catheter—a tubular device inserted into a canal, vessel, or body cavity for either the introduction or extraction of some material

Chloroplast—a specialized body (a plastid) containing chlorophyll in the cytoplasm of plants; the site of photosynthesis and starch formation in plants

Chlorosis—a disease condition in green plants, marked by yellowing or blanching

Chronaxie (chronaxy)—the minimum time required for the excitation of a nervous element by a specified stimulus

Cilium (pl. *cilia*)—small, hairlike process attached to a free surface of a cell, capable of rhythmic movement

Clearance—the removal of material from the body or from an organ

Concentration—the total mass (usually in micrograms) of the suspended particles contained in a unit volume (usually one cubic meter) at a given temperature and pressure; sometimes, the concentration may be expressed in terms of total *number* of particles in a unit volume (e.g., parts per million); concentration may also be called the "loading" or the "level" of a substance; concentration may also pertain to the strength of a solution

Conductometric—a method of analysis based on the conductivity of a sample

Conifer—belonging to the coniferales order, consisting primarily of evergreen trees and shrubs

Conjunctiva—the delicate membrane lining the eyelids and covering the exposed surface of the eyeball

Conjunctivitis—an inflammation of the conjunctiva

Consolidation—the process by which a diseased lung passes from an aerated collapsible state to one of an airless solid consistency because of accumulation of exudate

Criteria, air quality—a compilation of the scientific knowledge of the relationship between various concentrations of pollutants in the air and their adverse effects

Deciduous—falling off or shed at the end of a growing period or season

Deliquesce—to dissolve gradually and become liquid by absorbing moisture from the air

Desorption—the release of a substance which has been taken into another substance by a physical process or held in concentrated form upon the surface of another substance; the reverse of absorption or adsorption

Desquamate—to cast off epidermis in shreds or scales; to peel off in sheets or scales

Diameter, count median (CMD)—the geometric median size of a distribution of particles, based on a numerical count

Diameter, mass median (MMD)—the geometric median size of a distribution of particles, based upon a weight (usually derived from a Stokes' Diameter)

Dichotomous—dividing in succession into pairs; showing a dual arrangement

Distal—furthest or most remote from the median line of the body, from the point of attachment, or from the origin; peripheral (*cf.* proximal)

Dolomite—a limestone or marble rich in magnesium carbonate

Dyspnea—difficult or labored breathing

Edema—a condition due to the presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body

Effusion—the escape of fluid into a tissue or part, usually by the rupture of a vessel or extravasation through its walls

Electroencephalogram (EEG)—a graphic recording of electric currents developed in the brain, obtained with the use of electrodes which are usually applied to the scalp

Emphysema—a swelling due to the presence of air, usually excess or additional air. The term is usually used to refer to pulmonary emphysema

Emphysema, pulmonary—a condition in which there is overdistension of air spaces and resultant destruction of alveoli and loss of functioning lung tissue

Epidemiology—a science dealing with the factors involved in the distribution and frequency of a disease pr[illegible] a population

Epidermis—the outermost layer [illegible] in animals; any integument

Epithelium—a closely packed sheet of cells arranged in one or more layers, covering the surface of the body and lining hollow organs

Exacerbation—an increase in the severity of any symptoms or of a disease

Exteroceptive—activated by or relating to any stimulus impinging on an organism from the outside

Fibrosis—the development of fibrous tissue; sclerosis

Filiform—having the shape of a thread or filament

Follicle (follicule)—a very small excretory or secretory sac or a small gland

Gallamine—a drug used to relax skeletal muscles

Gneiss—a laminated or foliated metamorphic rock

Goblet cell—a type of epithelial cell containing mucus and having the shape of a flask or goblet

Halide—any binary compound of a halogen

Halogen—any one of the chemically related elements fluorine, chlorine, bromine, iodine, and astatine

Hemoglobin—a protein found in red blood cells, responsible for oxygen transport to all parts of the body

Hilum (hilus)—a depression or pit at that part of an organ where the vessels and nerves enter

Histamine—a substance which produces dilatation of capillaries and stimulates gastric secretion, occurring in both animal and vegetable tissues; β-imidazol-ethylamine

Histology—the study of the anatomy of tissues and their microscopic cellular structure

Hydrocarbon—a compound containing only hydrogen and carbon. This group is subdivided into alicyclic, aliphatic, and aromatic hydrocarbons according to the arrangement of the atoms and the chemical properties of the compounds

Hygroscopic—readily absorbing and retaining moisture

Hypertrophy—an enlargement or overgrowth of an organ or tissue due to an increase in the size of its constituent cells

Impactor, cascade—an instrument which employs several impactions in series to collect successively smaller sizes of particles

Incidence—the rate at which a certain event or disease occurs

Intercostal—situated between ribs

Interoceptive—of or relating to any stimulus arising from within the body

Interstitial—pertaining to or situated in the space between cells

Isopleth—a line on a map connecting points at which a given variable has a specified constant value

Isoproterenol—a sympathomimetic drug which is used to relieve bronchoconstriction and which also can function as a cardiac stimulant

Lacrimation (lachrymation)—tear formation, especially in excess

Lamina propria—a connective tissue layer located just beneath the epithelial cells and basement membrane of many organs

Larch—a tree of the genus *Larix* or of the family Pinaceae

Larynx—the organ concerned with the production of the voice, situated at the upper end of the trachea

Leach—to dissolve out by the action of a percolating liquid

Lesion—an injury or other circumscribed pathologic change in a tissue

Lumen—the inner space of a hollow organ or tube

Lymphocyte—a variety of white blood cells which arises in the reticular tissue of lymph glands

Lymphoid cell—a mononuclear cell found in lymphoid tissue (such as the spleen, tonsil, lymph nodes), ultimately concerned with immunologic function

Mean, geometric (Mg)—a measure of central tendency for a log-normal distribution; the value of a given set of samples above which 50 percent of the values lie

Monochromatic light—a beam of light having some desired, narrow range of wavelengths

Monodisperse—characterized by particles of uniform size in a dispersed phase

Morbidity—the occurrence of a disease state

Morphology—a branch of biology dealing with the structure and form of living organisms

Mortaliy—the ratio of the total number of deaths to the total population, *or* the ratio of the number of deaths from a given disease to the total number of people having that disease

Mucosa—a mucous membrane

Mucus (adj. *mucous)*—the clear viscid secretion of a mucous membrane

Mural—pertaining to the wall of a cavity

Nasopharynx—the part of the pharynx (throat) lying above the level of the soft palate

Nebulize—to reduce to a fine spray

Necrosis—localized death of cells

Nembutal—a barbiturate drug used as a hypnotic and a sedative; pentobarbital

Node—a circumscribed swelling

Node, lymph—one of many accumulations of lymphatic tissue situated throughout the body

Nucleus (condensation nucleus)—a particle in the size range from 0.1μ to 1μ which serves as a nidus on which water or other vapors in the air can condense to form liquid droplets

Olefin—a class of unsaturated hydrocarbons of the general formula $C_n H_{2n}$

Olfactory—pertaining to the sense of smell

Optical—pertaining to vision

Oropharynx—that part of the pharynx (throat) lying between the level of the soft palate and the epiglottis

Paraffin—a purified mixture of solid hydrocarbons obtained from petroleum, occurring as an odorless, tasteless, colorless or white, relatively translucent mass

Parenchyma—the specific or functional tissue of a gland or organ, as opposed to its supporting framework

Pathogen—any disease-producing organism or material

Pathogenesis—the production or the mode of origin and development of a disease condition

Pathology—the study of the essential nature of disease, particularly with respect to the structural and functional changes in organs and tissues

Pharynx—the upper expanded portion of the alimentary canal lying between the mouth, the nasal cavities, and the beginning of the esophagus; the throat

Photochemistry—a branch of chemistry dealing with the effect of radiant energy (as light) in producing chemical changes

Photosynthesis—the formation of carbohydrate from carbon dioxide and water in the presence of chlorophyll and light, in plant tissues

Physiology—a science which studies the function of a living organism or its parts

Phytotoxic—harmful to plant materials

Plethysmograph—an apparatus for the determination and recording of a change in the size of an organ or limb or body

Pneumonitis—a general term for inflammation of the lung

Pneumotachygraph—an instrument used to determine the force and velocity of respired air

Potentiation—synergism, as between two agents which together have a greater effect than the sum of their effects when acting separately

Prevalence—the number of cases of a disease at a given time

Privet—any one of various plants of the genus *Ligustrum*, used extentively as ornamental shrubs

Procaine—a drug which is used primarily as a local anesthetic

Proximal—nearest to the center of the body or the point of origin (*cf.* distal)

Rale—an abnormal respiratory sound heard in auscultation of the chest

Ratio, standardized mortality—the ratio of the number of deaths observed in a given population over a given period of time *to* the number of deaths expected to occur in the given population over the same period of time if the given population behaved as any other group of similar composition would during that same period

Rhinitis—an inflammation of the nasal mucous membrane

Rhinorrhea—"runny nose"

Rhonchus (*pl.* rhonchi)—a dry, coarse sound usually originating from partial obstruction in a bronchial tube

Spasm—an involuntary and abnormal muscular contraction, usually sudden and forceful, and often accompanied by pain and/or loss of function

Spectroscopy—the branch of physical science dealing with the theory and interpretation of bands of light

Spirometer—an instrument for the measurement of the volume of gas respired by the lungs

Squamous—resembling or covered with scales

Standards, air quality—levels of air pollutants which can not legally be exceeded during a specific time in a specific geographical area

Subcutaneous—beneath the skin

Sympathetic—referring to the *sympathetic trunk* or the entire *sympathetic nervous system*, concerned with the involuntary regulation of cardiac muscle, smooth muscles, and glands

Synergism—a situation in which the combined action of two or more agents acting together is greater than the sum of the action of these agents separately

Systemic—relating to the body as a whole, rather than to its individual parts

Toxicology—the study of poisons, including their preparation, identification, physiologic action, and antidotes

Trachea—windpipe; the airway extending from the larynx to the origin of the two mainstem bronchi

Tracheotomy—a surgical opening through the skin and muscles of the neck into the trachea

Transpiration—the emission of water vapor from the surface of plant leaves

Vagosympathetic—referring to the parts of the nervous system with innervation by the vagus nerve and innervation through the sympathetic nervous system

Vagus—pertaining to either of the pair of tenth (X) cranial nerves, which supply parasympathetic, visceral afferent, motor, and general sensory innervation

Valence—an integer representing the number of hydrogen or chlorine atoms which one atom of an element is capable of combining with

Ventilation, minute—the total volume of gas respired in one minute, i.e., the tidal volume multiplied by breaths per minute.

Viscus (pl. viscera)—any internal organ within a body cavity

Visual range—the distance, under daylight conditions, at which the apparent contrast between the specified type of target and its background becomes just equal to the threshold contrast of an observer, i.e., the distance at which it is just possible to see a dark object against the sky near the horizon

Volume, forced expiratory (FEV)—the volume of gas forcibly exhaled over a given time interval (usually measured in seconds) after maximum inspiration, e.g., $FEV_{1.0}$ for this measurement over a one second period

Volume, minute—same as minute ventilation

Volume, tidal—the volume of gas inspired or expired during each respiratory cycle

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